William Ulwelling, M.D., M. P. H.

[redacted]

[redacted]

Medical Cannabis Program
William Catanech, Interim Program Manager
1190 St. Francis Dr Suite, Suite S-4207
Santa Fe, NM 87505
http://www.nmhealth.org/IDB/medical_cannabis.shtml

7/29/12

Dear Sir or Madam:

This petition concerns the currently approved condition of PTSD as an eligible condition for enrollment in the Medical Cannabis Program. I have enclosed two copies of this petition, which are written per the directives of the "New Mexico Department of Health Medical Cannabis Program Petition Requirements." (Note that the mailing address in the Petition Requirements lists an incorrect ZIP code for 1190 St. Francis Dr.)

At the next hearing of the Medical Cannabis Advisory Board on 10/17/12 I will petition the removal of Posttraumatic Stress Disorder (PTSD) from the list of eligible medical conditions for enrollment in the NM Medical Cannabis Program.

While these hearings before the Medical Cannabis Program generally consider the addition of new eligible medical conditions, Advisory Board Duties and Responsibilities also include, "Review conditions previously reviewed by the board and approved by the secretary for the purpose of determining whether to recommend the revision of eligibility criteria for persons applying under those conditions or to review new medical and scientific evidence pertaining to currently approved conditions. [underlining mine]" [Medical Use of Cannabis, Advisory Board Responsibilities and Duties 7.34.2.8.B(5)].

I will be the sole witness presenting testimony, and my personal contact information is noted above. I also include a copy of my New Mexico driver's license as verification of my New Mexico residence.

At the 10/17/12 Hearing I would like approximately 15 minutes to present technical evidence, and will offer into evidence the following five exhibits:
1. "Guideline Watch (March 2009): Practice Guideline for the Treatment of Patients with Acute Stress Disorder and Posttraumatic Stress Disorder," American Psychiatric Association Practice Guidelines, March, 2009
2. "Cannabis, Synthetic Cannabinoids, and Psychosis Risk: What the Evidence

Says," Pierre JM. Current Psychiatry, 2011; Vol. 10, No.9, 49-57
3. "Psychosis Associated With Medical Marijuana: Risk vs. Benefits of Medicinal Cannabis Use" Pierre JM. Am J Psychiatry 2010 167:5 (598-599)
4. "Medical Marijuana for the Treatment of Post Traumatic Stress Disorder: An Evidence Review." Campos-Outcalt D, University of Arizona, Report to The Arizona Department of Health Services, 2012.
5. "Disapprove Medical Marijuana as a Treatment for PTSD", Ulwelling W; Action Paper approved by the Assembly of the American Psychiatric Association, May 2012

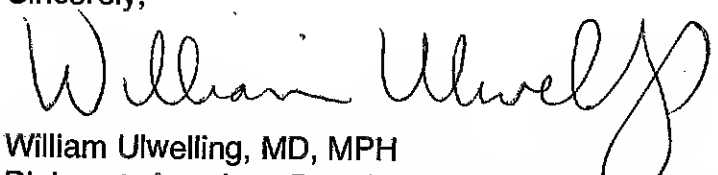
A summary of my testimony:

PTSD is a diagnosis defined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, published by the American Psychiatric Association. Recently updated practice guidelines from the APA include at least two dozen psychiatric medications that can claim at least some degree of evidence-based medical justification for treatment of PTSD. Cannabis is not included in these medications. Cannabis is not approved for the treatment of PTSD, or any psychiatric disorder (Cf. exhibit 1). Furthermore, there are no scientific studies that offer proper evidence that marijuana treats PTSD (Cf. exhibit 4).

There is a recognized association between PTSD and cannabis, but the primary accepted association is that PTSD sufferers have an increased vulnerability to alcohol and substance abuse disorders, and have a higher incidence of cannabis abuse. Offering cannabis to a PTSD sufferer increases this risk of substance abuse. Recently, possibly due to the increased potency of available cannabis, there have been an increasing number of cases of psychosis (paranoia, hallucinations) among marijuana users, and marijuana is now considered to be a "component cause" of psychosis in these cases (Cf. exhibits 2,3). PTSD sufferers, whose symptoms can include flashbacks of psychotic intensity, are at risk for such psychotic side effects.

In the three years since New Mexico approved PTSD as an indication for medical marijuana, new studies have shown added risk of side effects, and new reviews have demonstrated the continued absence of scientific studies demonstrating benefit.

Sincerely,



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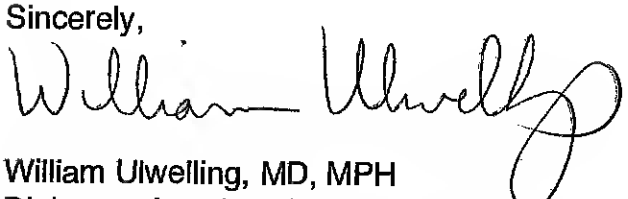

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NEW MEXICO

Exhibit 1

David M. Benedek, M.D.
Matthew J. Friedman, M.D., Ph.D.
Douglas Zatzick, M.D.
Robert J. Ursano, M.D.

Guideline Watch (March 2009): Practice Guideline for the Treatment of Patients with Acute Stress Disorder and Posttraumatic Stress Disorder

APA's *Practice Guideline for the Treatment of Patients with Acute Stress Disorder and Posttraumatic Stress Disorder* was published in October 2004. Since that time, a number of well-designed randomized controlled trials of pharmacological and psychotherapeutic interventions for posttraumatic stress disorder (PTSD) have been conducted in various populations exposed to trauma. Numerous case reports, small case series, and open trials have also been reported, but they will not be the focus of this guideline watch. While early intervention studies for acute stress disorder (ASD) are currently in progress, no major research on the treatment of ASD has been completed since publication of the 2004 guideline. Factors predicting development of ASD or PTSD have still not been established. A 2008 study by Bryant et al. (1) found that ASD was a poorer predictor of getting PTSD than just having PTSD criteria alone in the acute stage. In response to increased attention on U.S. military veterans returning from combat in Iraq and Afghanistan, the Institute of Medicine has also reviewed and summarized the evidence supporting treatment for PTSD (2). The 2007 report recognizes that there is evidence for the pharmacological treatment of combat-related PTSD but states that this evidence is not as strong as the evidence for treatment of other trauma-related PTSD. In particular, the report states that large randomized controlled trials, considered a standard of evidence in other areas of medicine, are lacking from the evidence base. The report concludes that existing evidence is sufficient only to establish the efficacy of exposure-based psychotherapies in the treatment of PTSD. However, there was disagreement among the report authors about this conclusion, and the report includes a dissenting opinion by one author about the strength of the evidence for pharmacotherapy. Our review concludes that the best evidence from recent studies bolsters support for exposure-based psychotherapies as well as for pharmacological intervention in many circumstances. Emerging evidence suggests the potential for psychotherapy to be facilitated by at least one recently identified pharmacological agent (d-cycloserine). Recently published studies also suggest that in certain patient populations new pharmacotherapeutic options, such as prazosin, may be more effective than other widely prescribed medications (e.g., selective serotonin reuptake inhibitors [SSRIs]) indicated for PTSD. As described in the 2004 guideline, the generalizability of findings from available studies on treatments for PTSD is limited by small numbers of subjects, variable inclusion criteria (e.g., patients with treatment-resistant illness, patients receiving multiple treatments), nonstandardized outcome measures, inadequate controls, and lack of replication. These issues also limit meaningful comparison of data for psychopharmacological versus psychotherapeutic approaches. Specific recommendations to improve psychotherapy research for PTSD have been put forward by Schottenbauer et al. (3).

For the period from October 2007 to October 2008, Dr. Benedek reports no competing interests, Dr. Friedman reports receiving an honorarium from AstraZeneca for participating in a symposium, Dr. Zatzick reports no competing interests, and Dr. Ursano reports no competing interests. The Executive Committee on Practice Guidelines has reviewed this watch and found no evidence of influence from these relationships.

The American Psychiatric Association's (APA's) practice guidelines are developed by expert work groups using an explicit methodology that includes rigorous review of available evidence, broad peer review of iterative drafts, and formal approval by the APA Assembly and Board of Trustees. APA practice guidelines are intended to assist psychiatrists in clinical decision making. They are not intended to be a standard of care. The ultimate judgment regarding a particular clinical procedure or treatment plan must be made by the psychiatrist in light of the clinical data presented by the patient and the diagnostic and treatment options available. Guideline watches summarize significant developments in practice since publication of an APA practice guideline. Watches may be authored and reviewed by experts associated with the original guideline development effort and are approved for publication by APA's Executive Committee on Practice Guidelines. Thus, watches represent opinion of the authors and approval of the Executive Committee but not policy of the APA. This guideline watch was published in March 2009.

PHARMACOTHERAPIES

ANTIDEPRESSANTS

Selective serotonin reuptake inhibitors for non-combat-related PTSD. Meta-analyses and several randomized controlled trials published since 2004 generally support the superiority of SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs) over placebo for non-combat-related PTSD.

In a 2006 Cochrane meta-analysis, Stein et al. (4) reviewed 35 short-term randomized controlled trials (of 14 or fewer weeks in duration) involving a total of 4,597 participants. In 17 of the trials, symptom severity was significantly reduced in the medication groups relative to placebo. Evidence of efficacy was most convincing for the SSRIs, across all symptom clusters and for co-occurring depression and disability.

In a study reported in 2007, Marshall et al. (5) evaluated the efficacy of paroxetine for treating symptoms and associated features of chronic PTSD. Fifty-two mostly minority adult patients (out of 70 initially enrolled) who were rated as not significantly improved after 1 week of placebo were randomized to receive flexibly dosed paroxetine (maximum 60 mg/day by week 7) or continued placebo. After 10 weeks, significantly more patients treated with paroxetine responded to treatment, as rated by the Clinical Global Impression-Improvement (CGI-I) scale. Patients treated with paroxetine were also observed to have significantly greater reduction in total score on the Clinician-Administered PTSD Scale (CAPS) and the Dissociative Experience Scale; self-reported interpersonal problems were also noted to be significantly decreased. During a 10-week maintenance phase, paroxetine response but not placebo response continued to improve.

In a 2006 reanalysis of two previously published trials, Stein et al. (6) examined 395 adult patients with PTSD who were randomized to double-blind treatment with flexibly dosed sertraline (50–200 mg/day) or placebo. After 12 weeks, sertraline was significantly more effective than placebo on most primary efficacy variables including Part 2 of the CAPS, irrespective of whether the patients had experienced childhood abuse or interpersonal trauma, suggesting the utility of medication treatment in individuals whose precipitating trauma is either childhood abuse in particular or interpersonal trauma in general.

In a 2005 study, Davidson et al. (7) compared the relapse rates of 57 of 62 total patients who responded to 6 months of open-label fluoxetine and who were subsequently blindly randomized to continue receiving fluoxetine (mean dosage = 42.1 mg/day) or placebo. Relapse rates were 22% for fluoxetine compared with 50% for placebo ($p = 0.02$); the odds ratio for relapse on placebo relative to fluoxetine was 3.50, and time to relapse on fluoxetine was longer than on placebo ($p = 0.02$, log rank statistic).

These newer studies augment the evidence base for SSRI efficacy previously established in samples of predominantly women with PTSD resulting from civilian trauma, including childhood and adult sexual assault, other interpersonal traumas, and motor vehicle accidents.

SSRIs for combat-related PTSD. Randomized controlled trials have called into question the efficacy of SSRIs for the treatment of PTSD in combat veterans. Some of this evidence was described in the 2004 guideline, including van der Kolk et al.'s 1994 study (8) of 31 veterans with chronic PTSD randomized to fluoxetine or placebo. In this study, fluoxetine was significantly superior to placebo for symptoms of co-occurring depression as measured by the Hamilton Depression Rating Scale (HAM-D), but change in total PTSD score did not diffet between placebo and fluoxetine. In a similar randomization of 88 veterans with PTSD, none of those receiving 8 weeks of fluoxetine treatment achieved an asymptomic state as measured by the CAPS at 6-month follow-up (9). Negative results were reported in a placebo-controlled, randomized controlled trial by Hertzberg et al. (10) of fluoxetine in 12 Vietnam war veterans.

Mote recently, Friedman et al. (11) completed a multi-center trial of sertraline in 169 combat veterans with PTSD recruited from 10 Veterans Affairs medical centers. After 1 week of placebo, the patients wete randomized to receive 12 weeks of flexibly dosed serttaline (mean dosage = 156 mg/day among completers) or continued placebo. Total PTSD symptom reduction as measured by the CAPS did not significantly differ between the sertraline (−13.1, +/−3) and placebo (−15.4, +/−3.1) groups, and in both groups, combat-related PTSD was associated with poorer outcome compared with non-combat-related PTSD.

In a 2002 study, Zohar et al. (12) randomized 42 Israeli combat veterans to sertraline (mean dosage = 120 mg/day, +/−60 mg) or placebo. At 10 weeks, no significant differences were noted in total score on the CAPS-2 or on any of the three CAPS symptom cluster scores.

These findings stand in contrast to a 2006 randomized controlled trial by Martenyi and Soldatenkova (13) of 144 combat veterans of the Balkan Wars recruited at eight sites in Bosnia-Herzegovina

and Croatia and randomized to fluoxetine (20–80 mg/day) or placebo for both a 12-week acute phase and 24-week relapse prevention phase. In the acute phase, fluoxetine was superior to placebo as measured by total score on the Treatment Outcome PTSD (TOP-8) scale (−9.05 compared with −5.20; $p = 0.001$), total score on the CAPS (−31.12 compared with −16.07; $p < 0.001$), all CAPS subscores, and total score on the Davidson Trauma Scale (DTS). Fluoxetine was also more effective for depression as measured by the Montgomery-Åsberg Depression Rating Scale (MADRS) and for anxiety symptoms as measured by the Hamilton Anxiety Scale. In the relapse prevention phase of the trial, fluoxetine was superior to placebo in sustaining improvement in TOP-8 and CAPS scores, and the risk of relapse was significantly greater in the placebo arm than in the fluoxetine arm (log rank test $\chi^2 = 4.9$, $df = 1$, $p = 0.048$). The veterans of the Balkan Wars were younger than the Israeli and American combat veterans (mean age = 36), somewhat more recently traumatized (although mean duration from index trauma was 6–7 years), and had likely received less treatment for their symptoms prior to study entry. It is possible that negative results with older combat veterans (in contrast to positive results with fluoxetine among younger veterans of the Balkan Wars) may be due to the chronicity of their PTSD (and co-occurring disorders) rather than a unique resistance to SSRI treatment among individuals with combat-related PTSD.

The 2004 guideline recommends the SSRIs as a first-line medication treatment for patients with PTSD. The trials reviewed above suggest that the SSRIs may no longer be recommended with the same level of confidence for veterans with combat-related PTSD as for patients with non-combat-related PTSD. Further research is needed to answer why these populations have been shown to have differential responses to SSRI treatment.

Other antidepressants. Since publication of the 2004 guideline, several randomized, placebo-controlled trials of venlafaxine, one trial of mirtazapine, one trial of nefazodone, and one trial of buproprion have been reported, as well as several head-to-head comparisons of these medications with SSRIs.

In a 2006 study, Davidson et al. (14) randomly assigned 329 adult outpatients from 56 sites who had a primary diagnosis of PTSD with symptom duration of 6 months or longer and CAPS scores of 60 or greater to receive venlafaxine, extended release (37.5–300 mg/day), or placebo. At 24 weeks, mean changes in total CAPS score from baseline were −51.7 for the venlafaxine group compared with −43.9 for the placebo group ($p = 0.006$); improvement was significantly greater for the venlafaxine group in symptom cluster scores for reexperiencing ($p = 0.008$) and avoidance/numbing ($p = 0.006$) but not for hyperarousal. Remission rates (defined as a CAPS score of 20 or lower) were found to be 50.9% for venlafaxine and 37.5% for placebo ($p = 0.01$). A 12-week, multicenter double-blind trial (15) compared venlafaxine extended release (37.5–300 mg/day) to sertraline (25–200 mg/day) or placebo in adult outpatients with PTSD. Mean changes from baseline scores on tbe CAPS-SX17 (an abbreviated version of the CAPS) were −41.8, −39.4, and −33.9 for venlaxine, sertraline, and placebo, respectively, with only venlafaxine separating from placebo in a statistically significant manner ($p < 0.05$).

In a 2007 study, Becker et al. (16) found no between-group differences in 30 patients with civilian- or military-related PTSD who were randomized to placebo or buproprion, sustained release, in addition to usual pharmacological care. About half of these patients were already receiving an SSRI at the time of randomization.

In a 2004 study, Davis et al. (17) randomized 41 predominantly male combat veterans with PTSD to nefazodone or placebo. After 12 weeks, they found significant improvement in percentage change of total CAPS score from baseline in those receiving nefazodone compared with those receiving placebo in a repeated analysis of variance with last observation carried forward ($p = 0.04$, effect size = 0.6).

Finally, in a double-blind, randomized, placebo-controlled trial of 29 patients with PTSD reported in 2003 by Davidson et al. (18), mirtazapine (up to 45 mg/day) was found to be more effective than placebo on the Global Improvement item of the Short PTSD Rating Interview (SPRINT; but not on total SPRINT score, nor on DTS total score), as well as on the Structured Interview for PTSD and anxiety subscale of the Hospital Anxiety and Depression Scale.

Head-to-head comparisons of antidepressants. As described in the 2004 guideline, no significant differences among antidepressants, including the SSRIs, were found in the few head-to-head studies then available. Since that time, studies have been published comparing nefazodone and sertraline (19), venlafaxine and sertraline (15), the SNRI reboxetine and fluvoxamine (20), and fluoxetine, moclobemide, and tianeptine (21). These studies have generally demonstrated the superiority of antidepressants to placebo but have done little to clarify the relative utility of these different antidepressants.

In total, these data build on the relatively robust evidence basis for pharmacological treatment with antidepressant medications (particularly SSRIs and SNRIs for noncombat PTSD) as compared with other classes of medications. However, the data also suggest that more effective pharmacological treatments must be identified, particularly for veterans with combat-related PTSD. It is also important to note that comparison of other pharmacotherapies with the SSRIs and SNRIs is complicated by methodological differences in the available studies. While the SSRIs and SNRIs have mostly been studied in rigorous trials compared with placebo, other agents have been studied against "treatment as usual" conditions or as augmentation agents in patients with refractory illness.

ADRENERGIC AGENTS

Beta-blockers. As described in the 2004 guideline, a potential role fot propranolol in preventing PTSD was suggested by a pilot study teported in 2002 by Pitman et al. (22), in which 32 emergency department patients received a 10-day course of propranolol or placebo, beginning within 6 hours of a trauma. Propranolol treatment did not change CAPS scores at 1 month but did decrease physiological response to script-driven imagery 3 months after the trauma. However, a 14-day randomized controlled trial reported in 2007 by Stein et al. (23) of propranolol compared with gabapentin compared with placebo failed to demonstrate the superiority of either medication over placebo.

Prazosin. Among the most promising advances in the pbarmacological tteatment of PTSD have been a series of placebo-controlled augmentation trials demonstrating the efficacy of the α-adrenergic antagonist prazosin for the treatment of trauma-related nightmares and sleep disruption (24–26). In these trials, patients were allowed to continue maintenance medications, including SSRIs, as the primary outcome variables were related to sleep distutbance rather than daytime PTSD symptoms. However, the studies also assessed total PTSD symptoms using either the CAPS or the PTSD Checklist-Civilian Version (PCL-C).

The first study, reported in 2003 by Raskind et al. (24), was a double-blind, crossovet ttial in which 10 Vietnam combat veterans with PTSD received placebo ot prazosin (mean dosage = 9.6 mg/night) over a 3-week dose-titration phase and a 6-week maintenance phase. Prazosin was significantly superior to placebo in reducing nightmares (CAPS "recurrent distressing dreams" item) and sleep disturbance (CAPS "difficulty sleeping" item) and in improving global clinical status (Clinical Global Impression of Change [CGIC]), with effect size z > 1.0 on all measures. Change in total CAPS score and scores on all three CAPS cluster items was also significantly greater with prazosin than with placebo.

The second study, reported in 2007 by Raskind et al. (25), was a parallel-group trial in 40 veterans with chronic PTSD, most of whom experienced combat-related trauma in Vietnam. Patients received placebo or prazosin (mean dosage = 13.3 mg/nigbt) during a 4-week dose-titration phase and an 8-week maintenance phase. Similar imptovements were observed in nightmares, sleep disturbance, and CGIC scores (effect size = 0.9). A numerically greater reduction in total CAPS score was observed with prazosin, but this did not reach statistical significance.

Finally, in a double-blind, placebo-controlled cross-over study of 13 civilians with trauma-related PTSD, reported in 2008 by Taylor et al. (26), prazosin was rapidly titrated to 3 mg/night during each 3-week treatment phase. Along with clinical outcomes, sleep time and sleep latency were recorded in the final 3 nights of the treatment phase. Total sleep time was 94 minutes longer with prazosin than with placebo (374 +/− 86 minutes compared with 280 +/− 105 minutes, $p < 0.01$, effect size = 0.98), and total rapid eye movement (REM) sleep and mean REM duration were also longer with prazosin. Once again, reductions in trauma nightmares, total PTSD symptoms (using the PCL-C) and CGIC scores were significantly changed compared with placebo.

Further investigation may clarify an optimal dosage and titration for prazosin, which based on the above studies appears to be effective in a range of 3–15 mg/nigbt. Clinically, a low dose could be tried and then increased if response is inadequate. Long-term efficacy has not been established.

Second-generation (atypical) antipsychotic medications. In 2006, Padala et al. (27) reported the results of a small pilot study in which 20 women ages 19–94 years with PTSD from sexual and domestic abuse were randomized during the acute phase to receive risperidone or placebo. A significant difference was observed between baseline and subsequent visit TOP-8 total scores beginning in week 6 and persisting through the 12th week of the study. This response pattern was also observed in the secondary outcome measures of CAPS, the HAM-D, and the Hamilton Anxiety Scale.

Risperidone was also studied in an 8-week randomized conttolled trial reported in 2004 by Reich et al. (28) of 19 women who met DSM-III-R criteria related to childhood abuse. Significant differences in reduction from baseline total CAPS-2 score ($z = -2.44$, $p = 0.015$) and significant re-

ductions in CAPS-2 intrusive ($z = -5.71$, $p < 0.001$) and hyperarousal ($z = -2.74$, $p = 0.006$) subscores were associated with flexible dosing (0.5–8 mg/day) of risperidone. In 2008, Rothbaum et al. (29) randomized 25 adult PTSD patients whose symptoms did not remit (<70% decrease in symptoms, as measured by the CAPS) with 8 weeks of open-label sertraline to augmentation with risperidone compared with placebo for an additional 8 weeks. Patients receiving placebo and risperidone did not differ in their continued improvement in symptoms of depression or PTSD over the 8 weeks of augmentation (both groups improved), although those who received rispetidone showed more improvement on the DTS sleep item on post hoc analysis.

Another second-generation (atypical) antipsychotic trial of note is a randomized, placebo-controlled augmentation study of 73 combat veterans reported in 2005 by Bartzokis et al. (30). This trial demonstrated risperidone's superiority to placebo in increasing response to SSRIs. These findings are consistent with the limited evidence from previous small randomized controlled trials of risperidone (31) and olanzapine (32).

In summary, these data are encouraging for adjunctive treatment with a second-generation antipsychotic in patients who have partially responded to an SSRI or an SNRI, including for co-occurring psychotic symptoms. As recommended in other APA practice guidelines (33), patients receiving an antipsychotic medication should be monitored for side effects including weight gain and metabolic changes.

Anticonvulsants. Randomized controlled trials of anticonvulsant medications remain extremely limited in number and have shown mixed results. In a study reported in 2007 by Tucker et al. (34), 38 civilian patients with PTSD were randomized to placebo or flexibly dosed topiramate (25–400 mg/day); there were no significant differences in total CAPS scores or total Clinical Global Impression Scale scores, although patients treated with topiramate demonstrated clinically significant decreases in TOP-8 total score and CAPS re-experiencing symptoms subscale score.

In a continuation study reported in 2006 by Connor et al. (35), 29 patients with PTSD who completed an open-label trial of tiagabine and demonstrated at least minimal improvement were randomized to continued tiagabine or placebo. Benefits of treatment were maintained in the tiagabine group, and tiagabine was associated with a greater trend toward remission, but there was no statistically significant difference in remission rates, nor was there a change in rate of relapse in comparison with the placebo group.

In 2007, Davidson et al. (36) also evaluated the efficacy of tiagabine (2–4 mg/day in divided doses) in a 12-week randomized, placebo-controlled, multisite trial of 232 adult patients with PTSD. They found neither a statistically significant change from baseline CAPS score in either group nor a significant difference in any other outcome measure including CGIC, TOP-8, Davidson Trauma scale, or MADRS. Thus, while the small, open-label trial of Connor et al. (35) suggested efficacy of tiagabine, this larger randomized controlled trial failed to confirm this.

Most recently, Davis et al. (37) randomized 85 older male military veterans with PTSD to an 8-week trial of divalproex compared with placebo. No difference in outcomes was noted for either group, and no improvement was noted.

Despite the fact that anticonvulsant medications have been well tolerated in all studies and despire the promising results of some open-label studies, limited evidence of efficacy precludes any recommendations for change in practice.

PSYCHOTHERAPIES

Nearly all of the randomized controlled trials of psychotherapy published since 2004 have examined interventions that many experts consider to be components of cognitive-behavioral therapy (CBT). As described in the 2007 report of the Institute of Medicine (2), therapeutic approaches and techniques overlap across psychotherapies, and there is no consensus on how these psychotherapies should be categorized. This review follows the approach of the Institute of Medicine report, grouping approaches and techniques as follows: CBTs that include elements of exposure, eye-movement desensitization and reprocessing (EMDR), other psychotherapies, and group psychotherapy. Research published since 2004 supports, in particular, exposure-based CBTs such as cognitive processing therapy and prolonged exposure therapy as effective treatments for PTSD when delivered in individual formats.

EXPOSURE-BASED CBTS

Trials of exposure-based CBTs conducted in the last several years generally included components of psychoeducation, breathing, and relaxation training. By definition, these exposure therapies also incorporated into the therapy sessions some form of reexposure to past traumatic experience (e.g., imaginal, in vivo, directed therapeutic, written, verbal, or taped narrative recountings). In addition, homework was often included. The generalizability of

the results of many of these studies to typical clinical populations is limited by high dropout rates, lack of intention-to-treat analysis, and lack of clarity regarding blinding of assessors. Nevertheless, several well-designed studies augment prior knowledge.

In 2006, Monson et al. (38) reported the results of a waitlist-conttolled study of cognitive processing therapy in 60 combat veterans. The overall dropout tate was 16.6% (20% from cognitive processing therapy, 13% from waitlist), but random regression analyses of the intention-to-treat sample revealed significant improvements in both PTSD and co-occurring depressive symptoms in the treatment group compared with the waitlist group. At completion of the study, 40% of those in the intention-to-treat group receiving cognitive processing therapy no longer met criteria for a PTSD diagnosis, and 50% had a reliable decrease in their PTSD symptoms.

The effectiveness of cognitive processing therapy was also examined in a controlled study reported in 2005 by Chard (39) of 71 adult sexual abuse survivors with PTSD. The control was a minimal-attention waitlist group. Participants were assessed pretreatment, immediately after treatment, 3 months after tteatment, and 1 year after treatment using the CAPS and a variety of other clinician-administered rating scales. Analysis demonstrated that cognitive processing therapy was supetior to waitlist in reducing PTSD symptoms and that reductions were maintained for at least 1 year.

A recent study by Resick et al. (40) attempted to dismantle the components of cognitive processing therapy and determine theit relative contributions to tteatment efficacy. In this study, 150 adult women with PTSD were randomized into one of three conditions: 1) full cognitive processing therapy, which included both exposure (i.e., writing and reading a detailed account of the trauma) and cognitive therapy (i.e., challenging patient assertions about the meaning of the trauma and the implications for the patient's life); 2) cognitive therapy without the writing and reading component; and 3) the writing and reading component without cognitive therapy. All conditions included 2 hours of thetapy per week for 6 weeks. Patients were assessed for PTSD (using CAPS) and depression in a blinded manner weekly, 2 weeks after the last session of therapy, and at 6 months. At the conclusion of the study, all treatment completers still met criteria for PTSD. However, substantial improvement was observed in all three treatment groups on primary PTSD and depression outcomes as well as on secondary measures of anxiety, guilt, and shame. Cognitive therapy without exposure was associated with gteater improvement than the exposure-only condition, suggesting that the cognitive component of this therapy (i.e., altering the meaning of the traumatic event) may be an active treatment mechanism that may occur without repeated and explicitly evoked fear memories. It also suggests that cognitive processing therapy might be characterized as a more cognitive than exposure-based therapy. Similar dismantling studies are under way and will be important to further clarify the active components of various psychotherapies for PTSD. Research questions include how cognitive components as compared with exposure components may be variably effective depending on factors such as the stage of the disorder (e.g., early compared with late), the presence of particular symptoms (e.g., dissociation, high levels of arousal, avoidance), and, of course, therapist variables.

Prolonged exposure therapy was studied in a randomized controlled trial reported in 2007 by Schnurr et al. (41) of female veterans (N = 277) and active duty personnel (N = 7) across 12 sites specializing in medical treatment for military veterans, including nine Veterans Affairs hospitals, two Veterans Affairs counseling centers, and one military hospital. Patients were randomly assigned to receive prolonged exposure therapy (N = 141) or present-centered therapy (N = 143) delivered in 10 weekly 90-minute sessions. Blinded assessors collected data before and immediately aftet treatment and 3 and 6 months aftet tteatment. Immediately aftet treatment, the prolonged exposure group was more likely than the present-centered therapy group to no longet meet PTSD criteria (41% compared with 27.8%, odds ratio [OR] = 1.80, confidence interval [CI] = 95%) and more likely to achieve full remission (15.2% compared with 6.9%, OR = 2.43, CI = 95%). These results were maintained at 3- and 6-month follow-up. It should be noted that although this was a study of military personnel and veterans, 70% of participants indicated sexual trauma as their index (worst) traumatic experience, and there was a 17% differential dropout rate between prolonged exposure and present-centered therapy, with more participants dropping out of the prolonged exposure arm.

A controlled study reported in 2005 by Rothbaum et al. (42) evaluated the relative efficacy of prolonged exposure therapy and EMDR. In this study, 74 adult female rape victims (index rape occurring either in adulthood or childhood) were randomized into 9-session prolonged exposure, EMDR, and waitlist control groups. Dropout rates across the groups were not significantly different (13% prolonged exposure, 20% EMDR, 16.7% waitlist). Immediately following treatment, the

groups receiving prolonged exposure and EMDR both demonstrated statistically significant improvement across three outcome measures, including a 50% or more decrease from baseline in CAPS score ($p = 0.001$). Posttreatment, 95% of participants who received prolonged exposure therapy and 75% of participants who received EMDR no longer met criteria for PTSD, and individuals who received both treatments showed significantly reduced depressive symptoms and dissociative symptoms immediately and at 6 months. Results were maintained at 6-month follow-up for the prolonged-exposure group across PTSD, depressive, and dissociative symptoms but maintained to a significantly lesser extent for the EMDR group with regard to PTSD.

The effectiveness of brief exposure therapy has been demonstrated in two recent studies reported in 2005 and 2007 by Basoglu et al. (43, 44). In the first study, 59 earthquake survivors with PTSD assessed by CAPS were randomized to a single-session exposure-based behavioral therapy intervention (in which the intensity of simulated trauma was adjusted in accordance with the patient's personal feelings of comfort) or to a waitlist (43). At 6, 12, and 24 weeks posttreatment, as well as at 1–2 years posttreatment, the treatment group was observed to have significant decreases in CAPS score, Beck Depression Inventory (BDI) score, and other patient self-measures of fear, anxiety, or overall impression. With regard to CAPS, effect sizes were considerable (Cohen's $d = 0.7–1.4$), and improvement rate rose from 49% at week 6 to over 80% at other assessment points.

In the second study (44), 31 earthquake survivors with PTSD were randomized to a single-session exposure-based behavioral therapy ($N = 16$) or to repeated assessments ($N = 15$). Participants were assessed at 4, 8, 12, and 24 weeks posttreatment and again after 1–2 years. Again, significant between-group treatment effects were observed in PTSD (assessed by CAPS) and assessor-rated global improvement (Global Improvement Scale-Assessor [GIS-A]), with significant between-group treatment effects observed in both outcome measures at week 8. Improvement rates of 40% at week 4 rose to 80% by week 24 and at 1–2 year follow-up, with large effect sizes (Cohen's $d = 0.9–1.7$) noted across primary measures at week 8.

EMDR

EMDR continues to be examined as a treatment for victims of trauma; however, many of the studies published since 2004 include participants without a formal PTSD diagnosis. An exception is a study reported in 2007 by van der Kolk et al. (9), in which 88 patients with PTSD were randomly assigned to 8 weeks of EMDR, fluoxetine, or placebo. Symptoms were assessed using the CAPS and BDI-II immediately posttreatment and at 6 months. At 6-month follow-up, 75% of the adult-onset (compared with 33% of the childhood-onset) patients receiving EMDR achieved remission as compared to none of the patients receiving fluoxetine. Neither treatment produced complete symptom remission in the majority of the patients with childhood-onset PTSD. It should be noted that fluoxetine was discontinued at termination of the 8-week treatment phase, so the poor SSRI outcomes at 6 months should not be surprising.

Another exception is a study reported in 2007 by Högberg et al. (45) of 24 transportation workers who had either been assaulted or who had witnessed a person-under-train accident and who met DSM-IV criteria for PTSD. Participants were randomized to either five sessions of EMDR or to a waitlist. After treatment, eight of 13 patients receiving EMDR (67%) no longer met criteria for PTSD compared with one of 11 (11%) patients on the wait-list ($p = 0.02$). Significant differences were also observed in Global Assessment of Functioning and HAM-D scores.

Neither of these studies dismantled the effects of exposure compared with eye-movement components of the treatment. Previous studies (summarized in the 2004 guideline) have shown the eye movements not to be critical to the treatment effect. These small studies suggest efficacy of brief EMDR in sexual assault victims and witnesses to vehicular accidents but cannot be generalized to combat veterans.

OTHER PSYCHOTHERAPIES

Since publication of the 2004 guideline, studies of other types of psychotherapy, including coping skills therapy, eclectic psychotherapy, psychodynamic psychotherapy, cognitive restructuring, and brainwave neurofeedback, have also been published, but the utility and generalizability of conclusions from these studies are limited by methodological issues such as lack of formalized diagnostic procedures, inclusion of non-PTSD patients, very high dropout rates, unspecified handling of dropouts or missing data, and lack of blinding of assessors. A study reported in 2004 by Neuner et al. (46) of coping skills therapy in 43 war refugees was methodologically sound but failed to demonstrate a differential effect of treatment. As noted in the 2004 guideline, although controlled studies of psychodynamic psychotherapy are lacking, clinical

consensus reflects the idea that a psychodynamic approach is useful in helping the patient integrate past traumatic experience(s) into a more adaptive or constructive schema of risk, safety, prevention, and protection, thereby reducing core symptoms of PTSD.

Case reports (47, 48) have recently suggested that exposure-based therapy may be facilitated through the use of computerized audio-visual simulations of a traumatic combat environment. The effectiveness of this facilitated CBT—termed "virtual reality therapy"—in disaster workers with PTSD has also been demonstrated in a small controlled trial. In 2007, Difede et al. (49) assigned 21 September 11 terrorist attack workers to either virtual reality treatment (N = 13) or waitlist control (N = 8). The treatment group showed a significant decline in CAPS scores compared with the waitlist group. While these reports are encouraging, larger randomized controlled trials must replicate such findings before virtual reality therapy can be recommended with the highest levels of confidence.

Group psychotherapy. The majority of psychotherapies may be delivered in either individual or group formats. Of the studies reviewed above, the 2005 study by Chard (39) comparing cognitive processing therapy to minimal attention waitlist used both individual and group therapy formats (participants in the treatment group received both individual and group therapy in the first 9 weeks, followed by 7 weeks of group therapy, then one session of individual therapy). Effects of group therapy compared with individual therapy were not clearly demonstrated in this study. While there is a substantial descriptive literature for group therapy for PTSD, well-designed studies of cognitive processing therapy and other psychotherapies delivered in group formats are needed in the future in order to validate the efficacy of this method of delivery.

Psychological First Aid

The 2004 guideline described the failure of psychological debriefing as an effective strategy for preventing the later development of PTSD. There is hope that a new preventive approach for disaster survivors, called "psychological first aid," will prove effective (50). The essential principles of psychological first aid, including fostering safety, calmness, self- and community efficacy, social connectedness, and optimism in the aftermath of disaster, are supported by considerable empirical evidence, comprehensively summarized in 2007 by Hobfoll et al. (51). However, questions remain regarding how a public health intervention such as psychological first aid should be delivered, including which format and which type of respondent (clinician responder compared with emergency responder compared with community leader) would be optimal (52). Thus, at the present time, psychological first aid must be considered an evidence-informed rather than evidence-based intervention. Further research is needed.

Neurobiology of PTSD: Implications for Treatment

In addition to the intervention studies reviewed here, other recently published studies and articles are noteworthy for advancing our understanding of the neurobiology of the traumatic stress response and PTSD as they relate to the processes of emotional memory and impairment of extinction learning (53–56). These studies provide a theoretical basis for the mechanism of action of exposure-based CBTs as interventions that promote reprocessing and reconsolidation of emotionally laden memories of traumatic experiences and facilitate the extinction of conditioned responses to reminders of these experiences. Studies also point to the involvement of *N*-methyl-D-aspartate (NMDA) receptors in the process of extinction learning, suggesting a potential role for NMDA agonists as enhancers of exposure-based psychotherapies (57, 58). Trials under way at this time may augment the emerging data from pilot studies that suggest the possible benefits of NMDA agonist treatment in combination with exposure-based psychotherapies (59). However, to date there have been no published studies of using d-cycloserine or any other pharmacological agent to enhance response to psychotherapy in patients with PTSD.

Conclusion

Since publication of the 2004 guideline, increasing research attention has been focused on the assessment and treatment of PTSD, but much work remains to be done. The studies highlighted in this watch suggest that future psychotherapy research must rely on increasingly standardized mechanisms for addressing treatment dropouts and missing data, as well as standardized definitions of treatment outcome and remission. For generalizability to clinical populations, studies inclusive of co-occurring conditions—particularly other mood and anxiety disorders—and more studies addressing cross-cultural and multiethnic populations are necessary. Further studies may help to clarify the effects of psychological trauma occurring in childhood and adolescence, not only as this pertains to the treatment of PTSD but also with regard to other aspects of psychological functioning (including

personality) in adulthood. Although recent studies suggest that exposure-based psychotherapies may be effective for returning combat veterans, effectiveness studies also remain necessary in populations with co-occurring substance abuse or with other general medical and mental disorders (particularly traumatic brain injury). One study of collaborative care suggests that care management in combination with evidence-based psychotherapy and medication treatment may diminish PTSD symptoms in acutely injured trauma survivors (60).

With the exception of the α-adrenergic antagonist prazosin, the evidence base for pharmacological intervention in combat-related PTSD has not been significantly augmented by recent studies. Indeed, these studies suggest that SSRIs may not be recommended with the previous level of confidence for the treatment of PTSD in this particular population. Recent data point more to the need for replication of previous studies in typical clinical populations, the use of more standardized measures of outcome, and the need to identify alternative pharmacological strategies and to clarify the possibility that existing types of psychotherapy might be specifically augmented by novel pharmacological agents or other forms of intervention.

Finally, as epidemiological studies continue to demonstrate that there are increasing numbers of disaster victims and returning combat veterans with PTSD, it is crucial to support and expand efforts to identify effective delivery methods that can increase access to care, including group therapies, Internet- and self-help-based treatments, and treatments integrated into primary care practice environments (61–64). Further epidemiological studies will help identify risk factors and clarify the natural course of the illness, the impact of early intervention on the trajectory of illness, and the relationship between ASD and PTSD.

REFERENCES

1. Bryant RA, Creamer M, O'Donnell ML, Silove D, McFarlane AC: A multisite study of the capacity of acute stress disorder diagnosis to predict posttraumatic stress disorder. J Clin Psychiatry 2008; 69:923–929
2. Institute of Medicine: Treatment of PTSD: An Assessment of the Evidence. Washington, DC, National Academies Press. http://www.iom.edu/?id=47402, 2007
3. Schottenbauer MA, Glase CR, Arnkoff DB, Tendick V, Gray SH: Nonresponse and dropout rates in outcome studies on PTSD: review and methodological considerations. Psychiatry 2008; 71:134–168
4. Stein DJ, Ipser JC, Seedat S: Pharmacotherapy for post traumatic stress disorder (PTSD). Cochrane Database Syst Rev 2006;CD002795
5. Marshall RD, Lewie-Fernandez R, Blanco C, Simpson HB, Lin SH, Vermes D, Garcia W, Schneier F, Neria Y, Sanchez-Lacay A, Liebowitz MR: A controlled trial of paroxetine for chronic PTSD, dissociation, and interpersonal problems in mostly minority adults. Depress Anxiety 2007; 24:77–84
6. Stein DJ, van der Kolk BA, Austin C, Fayyad R, Clary C: Efficacy of sertraline in posttraumatic stress disorder secondary to interpersonal trauma or childhood abuse. Ann Clin Psychiatry 2006; 18:243–249
7. Davidson JR, Connor KM, Hertzberg MA, Weisler RH, Wilson WH, Payne VM: Maintenance therapy with fluoxetine in posttraumatic stress disorder: a placebo-controlled discontinuation study. J Clin Psychopharmacol 2005; 25:166–169
8. van der Kolk BA, Dreyfuss D, Michaels M, Shera D, Berkowitz R, Fisler R, Saxe G: Fluoxetine in posttraumatic stress disorder. J Clin Psychiatry 1994; 55:517–522
9. van der Kolk BA, Spinazzola J, Blaustein ME, Hopper JW, Hopper EK, Korn DL, Simpson WB: A randomized clinical trial of eye movement desensitization and reprocessing (EMDR), fluoxetine, and pill placebo in the treatment of posttraumatic stress disorder: treatment effects and long-term maintenance. J Clin Psychiatry 2007; 68:37–46
10. Hertzberg MA, Feldman ME, Beckham JC, Kudler HS, Davidson JR: Lack of efficacy for fluoxetine in PTSD: a placebo controlled trial in combat veterans. Ann Clin Psychiatry 2000; 12:101–105
11. Friedman MJ, Marmar CR, Baker DG, Sikes CR, Farfel GM: Randomized, double-blind comparison of sertraline and placebo for posttraumatic stress disorder in a Department of Veterans Affairs setting. J Clin Psychiatry 2007; 68:711–720
12. Zohar J, Amital D, Miodownik C, Kotler M, Bleich A, Lane RM, Austin C: Double-blind placebo-controlled pilot study of sertraline in military veterans with posttraumatic stress disorder. J Clin Psychopharmacol 2002; 22:190–195
13. Martenyi F, Soldatenkova V: Fluoxetine in the acute treatment and relapse prevention of combat-related posttraumatic stress disorder: analysis of the veteran group of a placebo-controlled, randomized clinical trial. Eur Neuropsychopharmacol 2006; 16:340–349
14. Davidson J, Baldwin D, Stein DJ, Kuper E, Benattia I, Ahmed S, Pedersen R, Musgnung J: Treatment of posttraumatic stress disorder with venlafaxine extended release: a 6-month randomized controlled trial. Arch Gen Psychiatry 2006; 63:1158–1165
15. Davidson J, Rothbaum BO, Tucker P, Asnis G, Benattia I, Musgnung JJ: Venlafaxine extended release in posttraumatic stress disorder: a sertraline- and placebo-controlled study. J Clin Psychopharmacol 2006; 26:259–267
16. Becker ME, Hertzberg MA, Moore SD, Dennis MF, Bukenya DS, Beckham JC: A placebo-controlled trial of bupropion SR in the treatment of chronic posttraumatic stress disorder. J Clin Psychopharmacol 2007; 27:193–197
17. Davis LL, Jewell ME, Ambrose S, Farley J, Englieh B, Bartolucci A, Petty F: A placebo-controlled study of nefazodone for the treatment of chronic posttraumatic stress disorder: a preliminary study. J Clin Psychopharmacol 2004; 24:291–297
18. Davidson JR, Weisler RH, Butterfield MI, Casat CD, Connor KM, Barnett S, van Meter S: Mirtazapine vs. placebo in posttraumatic stress disorder: a pilot trial. Biol Psychiatry 2003; 53:188–191
19. McRae AL, Brady KT, Mellman TA, Sonne SC, Killeen TK, Timmerman MA, Bayles-Dazet W: Comparison of nefazodone and sertraline for the treatment of posttraumatic stress disorder. Depress Anxiety 2004; 19:190–196
20. Spivak B, Strous RD, Shaked G, Shabash E, Kotler M, Weizman A: Reboxetine versus fluvoxamine in the treatment of motor vehicle accident-related posttraumatic stress disorder: a double-blind, fixed-dosage, controlled trial. J Clin Psychopharmacol 2006; 26:152–156
21. Onder E, Tural U, Aker T: A comparative study of fluoxetine, moclobemide, and tianeptine in the treatment of posttraumatic stress disorder following an earthquake. Eur Psychiatry 2006; 21:174–179
22. Pitman RK, Sanders KM, Zusman RM, Healy AR, Cheema F, Lasko NB, Cahill L, Orr SP: Pilot study of secondary prevention of posttraumatic stress disorder with propranolol. Biol Psychiatry 2002; 51:189–192
23. Stein MB, Kerridge C, Dimsdale JE, Hoyt DB: Pharmacotherapy to prevent PTSD: Results from a randomized controlled proof-of-concept trial in physically injured patients. J Trauma Stress 2007; 20:923–932
24. Raskind MA, Peskind ER, Kanter ED, Petrie EC, Radant A, Thompson CE, Dobie DJ, Hoff D, Rein RJ, Straits-Troster K, Thomas RG, McFall MM: Reduction of nightmares and other PTSD symptoms in combat veterans by prazosin: a placebo-controlled study. Am J Psychiatry 2003; 160:371–373
25. Raskind MA, Peskind ER, Hoff DJ, Hart KL, Holmes HA, Warren D, Shofer J, O'Connell J, Taylor F, Gross C, Rohde K, McFall ME: A parallel group placebo controlled study of prazosin for trauma nightmares and sleep disturbance in combat veterans with post-traumatic stress disorder. Biol Psychietry 2007; 61:928–934
26. Taylor FB, Martin P, Thompson C, Williams J, Mellman TA, Gross C, Peskind ER, Raskind MA: Prazosin effects on objective sleep measures and clinical symptoms in civilian trauma posttraumatic stress disorder: a placebo-controlled study. Biol Psychiatry 2008; 63:629–632
27. Padala PR, Madison J, Monnahan M, Marcil W, Price P, Ramaswamy S, Din AU, Wilson DR, Petty F: Risperidone monotherapy for post-traumatic

stress disorder related to sexual assault and domestic abuse in women. Int Clin Psychopharmacol 2006; 21:275–280
28. Reich DB, Winternitz S, Hennen J, Watts T, Stanculescu C: A preliminary study of risperidone in the treatment of posttraumatic stress disorder related to childhood abuse in women. J Clin Psychiatry 2004; 65:1601–1606
29. Rothbaum BO, Killeen TK, Davidson JR, Brady KT, Connor KM, Heekin MH: Placebo-controlled trial of risperidone augmentation for selective serotonin re-uptake inhibitor-resistant civilian posttraumatic stress disorder. J Clin Psychiatry 2008; 69:520–525
30. Bartzokis G, Lu PH, Turner J, Mintz J, Saunders CS: Adjunctive risperidone in the treatment of chronic combat-related posttraumatic stress disorder. Biol Psychiatry 2005; 57:474–479
31. Hamner MB, Faldowski RA, Ulmer HG, Frueh BC, Huber MG, Arana GW: Adjunctive ziprasidone treatment in post-traumatic stress disorder: a preliminary controlled trial of effects on comorbid psychotic symptoms. Int Clin Psychopharmacol 2003; 18:1–8
32. Stein MB, Kline NA, Matloff JL: Adjunctive olanzapine for SSRI-resistant combat-related PTSD: a double-blind, placebo-controlled study. Am J Psychiatry 2002; 159:1777–1779
33. American Psychiatric Association: Practice guideline for the treatment of patients with schizophrenia, second edition. Am J Psychiatry 2004; 161:1–56
34. Tucker P, Trautman RP, Wyatt DB, Thompson J, Wu SC, Capece JA, Rosenthal NR: Efficacy and safety of topiramate monotherapy in civilian posttraumatic stress disorder: a randomized, double-blind, placebo-controlled study. J Clin Psychiatry 2007; 68:201–206
35. Connor KM, Davidson JR, Weisler RH, Zhang W, Abraham K: Tiagabine for posttraumatic stress disorder: effects of open-label and double-blind discontinuation treatment. Psychopharmacology (Berl) 2006; 184:21–25
36. Davidson JR, Brady K, Mellman TA, Stein MB, Pollack MH: The efficacy and tolerability of tiagabine in adult patients with post-traumatic stress disorder. J Clin Psychopharmacol 2007; 27:85–88
37. Davis LL, Davidson JR, Ward LC, Bartolucci A, Bowden CL, Petty F: Divalproex in the treatment of posttraumatic stress disorder: a randomized, double-blind, placebo-controlled trial in a veteran population. J Clin Psychopharmacol 2008; 28:84–88
38. Monson CM, Schnurr PP, Resick PA, Friedman MJ, Young-Xu Y, Stevens SP: Cognitive processing therapy for veterans with military-related posttraumatic stress disorder. J Consult Clin Psychol 2006; 74:898–907
39. Chard KM: An evaluation of cognitive processing therapy for the treatment of posttraumatic stress disorder related to childhood sexual abuse. J Consult Clin Psychol 2005; 73:965–971
40. Resick PA, Galovski TE, O'Brien UM, Scher CD, Clum GA, Young-Xu Y: A randomized clinical trial to dismantle components of cognitive processing therapy for posttraumatic stress disorder in female victims of interpersonal violence. J Consult Clin Psychol 2008; 76:243–258
41. Schnurr PP, Friedman MJ, Engel CC, Foa EB, Shea MT, Chow BK, Resick PA, Thurston V, Orsillo SM, Haug R, Turner C, Bernardy N: Cognitive behavioral therapy for posttraumatic stress disorder in women: a randomized controlled trial. JAMA 2007; 297:820–830
42. Rothbaum BO, Astin MC, Marsteller F: Prolonged exposure versus eye movement desensitization and reprocessing (EMDR) for PTSD rape victims. J Trauma Stress 2005; 18:607–616
43. Basoglu M, Salcioglu E, Livanou M, Kalender D, Acar G: Single-session behavioral treatment of earthquake-related posttraumatic stress disorder: a randomized waiting list controlled trial. J Trauma Stress 2005; 18:1–11
44. Basoglu M, Salcioglu E, Livanou M: A randomized controlled study of single-session behavioural treatment of earthquake-related post-traumatic stress disorder using an earthquake simulator. Psychol Med 2007; 37:203–213
45. Högberg G, Pagani M, Sundin O, Soares J, Aberg-Wistedt A, Tärnell B, Hällström T: On treatment with eye movement desensitization and reprocessing of chronic posttraumatic stress disorder in public transportation workers—a randomized controlled trial. Nord J Psychiatry 2007; 61:54–61
46. Neuner F, Schauer M, Klaschik C, Karunakara U, Elbert T: A comparison of narrative exposure therapy, supportive counseling, and psychoeducation for treating posttraumatic stress disorder in an african refugee settlement. J Consult Clin Psychol 2004; 72:579–587
47. Wood DP, Murphy JA, Center KB, Russ C, McLay RN, Reeves D, Pyne J, Shilling R, Hegan J, Wiederhold BK: Combat related post traumatic stress disorder: a multiple case report using virtual reality graded exposure therapy with physiological monitoring. Stud Health Technol Inform 2008; 132:556–561
48. Gerardi M, Rothbaum BO, Ressler K, Heekin M, Rizzo A: Virtual reality exposure therapy using a virtual Iraq: case report. J Trauma Stress 2008; 21:209–213
49. Difede J, Cukor J, Jayasinghe N, Patt I, Jedel S, Spielman L, Giosan C, Hoffman HG: Virtual reality exposure therapy for the treatment of posttraumatic stress disorder following September 11, 2001. J Clin Psychiatry 2007; 68:1639–1647
50. Watson PJ, Gibson L, Ruzek JI: Public mental health interventions following disasters and mass violence, In Handbook of PTSD: Science and Practice. Edited by Friedman MJ, Keane TM, Resick PA. New York, Guilford Press, 2007, pp 521–539
51. Hobfoll SE, Watson P, Bell CC, Bryant RA, Brymer MJ, Friedman MJ, Friedman M, Gersons BP, de Jong JT, Layne CM, Maguen S, Neria Y, Norwood AE, Pynoos RS, Reissman D, Ruzek JI, Shalev AY, Solomon Z, Steinberg AM, Ursano RJ: Five essential elements of immediate and midterm mass trauma intervention: empirical evidence. Psychiatry 2007; 70:283–315
52. Benedek DM, Fullerton CS: Translating five essential elements into programs and practice. Commentary on "Five Essential Elements of Immediate and Mid-Term Mass Trauma Intervention: Empirical Evidence," by Hobfoll et al. Psychiatry: Biological and Interpersonal Processes 2007; 70:345–349
53. Quirk GJ, Garcia R, Gonzalez-Lima F: Prefrontal mechanisms in extinction of conditioned fear. Biol Psychiatry 2006; 60:337–343
54. Sharot T, Delgado MR, Phelps EA: How emotion enhances the feeling of remembering. Nat Neurosci 2004; 7:1376–1380
55. Wessa M, Flor H: Failure of extinction of fear responses in posttraumatic stress disorder: evidence from second-order conditioning. Am J Psychiatry 2007; 164:1684–1692
56. Guthrie RM, Bryant RA: Extinction learning before trauma and subsequent posttraumatic stress. Psychosom Med 2006; 68:307–311
57. Ressler KJ, Rothbaum BO, Tannenbaum L, Anderson P, Graap K, Zimand E, Hodges L, Davis M: Cognitive enhancers as adjuncts to psychotherapy: use of D-cycloserine in phobic individuals to facilitate extinction of fear. Arch Gen Psychiatry 2004; 61:1136–1144
58. Myers KM, Davis M: Mechanisms of fear extinction. Mol Psychiatry 2007; 12:120–150
59. Davis M, Myers KM, Chhatwal J, Ressler KJ: Pharmacological treatments that facilitate extinction of fear: relevance to psychotherapy. NeuroRx 2006; 3:82–96
60. Zatzick D, Roy-Byrne P, Russo J, Rivara F, Droesch R, Wagner A, Dunn C, Jurkovich G, Uehara E, Katon W: A randomized effectiveness trial of stepped collaborative care for acutely injured trauma survivors. Arch Gen Psychiatry 2004; 61:498–506
61. Kessler R, Brewin C, Galea S: Overview of baseline survey results: Hurricane Katrina Community Advisory Group. August 29, 2006. http://hurricanekatrina.med.harvard.edu/pdf/baseline_report%208-25-06.pdf, 2006
62. Ursano RJ: Individual and community responses to disasters, In Textbook of Disaster Psychiatry. Edited by Ursano RJ, Fullerton CS, Weisaeth L, Raphael B. Cambridge, UK, Cambridge University Press, 2008, pp 1–17
63. Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL: Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. N Engl J Med 2004; 351:13–22
64. Mental Health Advisory Team IV: IV Operation Iraqi Freedom 05–07 Final Report: 23–24. 2008. http://www.armymedicine.army.mil/reports/mhat/mhat_iv/mhat-iv.cfm

NOTES

Exhibit 2

Current PSYCHIATRY

Cannabis, synthetic cannabinoids, and psychosis risk: What the evidence says

Research suggests marijuana may be a 'component cause' of psychosis

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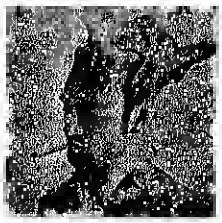
Over the past 50 years, anecdotal reports linking *cannabis sativa* (marijuana) and psychosis have been steadily accumulating, giving rise to the notion of "cannabis psychosis." Despite this historic connection, marijuana often is regarded as a "soft drug" with few harmful effects. However, this benign view is now being revised, along with mounting research demonstrating a clear association between cannabis and psychosis.

In this article, I review evidence on marijuana's impact on the risk of developing psychotic disorders, as well as the potential contributions of "medical" marijuana and other legally available products containing synthetic cannabinoids to psychosis risk.

Cannabis use and psychosis

Cannabis use has a largely deleterious effect on patients with psychotic disorders, and typically is associated with relapse, poor treatment adherence, and worsening psychotic symptoms.[1,2] There is, however, evidence that some patients with schizophrenia might benefit from treatment with cannabidiol,[3-5] another constituent of marijuana, as well as delta-9-tetrahydrocannabinol (Δ-9-THC), the principle psychoactive constituent of cannabis.[6,7]

The acute psychotic potential of cannabis has been demonstrated by studies that documented psychotic symptoms (eg, hallucinations, paranoid delusions, derealization) in a dose-dependent manner among healthy volunteers administered Δ-9-THC under ex-



Cannabis and psychosis

Clinical Point

Three meta-analyses have concluded cannabis use is associated with an increased risk of psychosis

Table 1

Hypotheses linking cannabis and psychosis

Hypothesis	Strength of evidence	Evidence for	Evidence against
Cannabis does not cause chronic psychosis	Weak	• No randomized controlled trials • Other possible explanations (demographic/socioeconomic, trauma, other drug use) • Possible reverse causality (psychosis leads to cannabis use) • Possible publication bias (negative evidence not published)	• Controlled (cross-sectional and longitudinal cohort) studies consistently show an association[11-19] • Longitudinal studies include risk calculations adjusted for confounding variables[13-19] • Publication bias not found in meta-analyses[11,21]
Cannabis can cause schizophrenia	Equivocal	Cannabis use precedes the onset of schizophrenia in longitudinal studies[13-19]	The incidence of schizophrenia has not been clearly increasing as expected with increasing cannabis use[11,21]
Cannabis worsens existing psychotic disorders	Strong	• Cannabis is associated with increased symptoms, relapse, and treatment nonadherence among those with schizophrenia[1,2] • Patients with schizophrenia are more vulnerable to cannabis-induced psychosis under experimental conditions[22]	Cannabidiol and Δ-9-THC improve symptoms in some patients with schizophrenia[3-7]
Cannabis increases the risk of chronic psychosis among vulnerable individuals	Strong	• For patients with schizophrenia, a history of cannabis use is associated with illness onset 2 to 3 years earlier compared with non-users[23] • Cannabis use is a risk factor for conversion to psychosis in some studies of prodromal schizophrenia[24]	Cannabis use is not always a risk factor for conversion to psychosis in studies of prodromal schizophrenia[25]

Δ-9-THC: delta-9-tetrahydrocannabinol

perimental conditions.[8-10] Various cross-sectional epidemiologic studies also have revealed an association between cannabis use and acute or chronic psychosis.[11,12]

In the absence of definitive evidence from randomized, long-term, placebo-controlled trials, the strongest evidence of a connection between cannabis use and development of a psychotic disorder comes from prospective, longitudinal cohort studies. In the past 15 years, new evidence has emerged from 7 such studies that cumulatively provide strong support for an association between cannabis use as an adolescent or young adult and a greater risk for developing a psychotic disorder such as schizophrenia.[13-19] These longitudinal studies surveyed for self-reported cannabis use before psychosis onset and controlled for a variety of potential confounding factors (eg, other drug use and demographic, social, and psychological variables). Three meta-analyses of these and other studies concluded an increased risk of psychosis is associated with cannabis use, with an odds ratio of 1.4 to 2.9 (meaning the risk of developing psychosis with any history of cannabis use is up to 3-fold higher compared with those who did not use cannabis).[11,20,21] In addition, this association appears to be dose-related, with increasing amounts of cannabis use linked to greater risk—1 study found an odds ratio of 7 for psychosis among daily cannabis users.[16]

There are several ways to explain the link between cannabis use and psychosis, and a causal relationship has not yet been firmly

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Table 2

Herbal incense products and synthetic cannabinoids

Herbal incense brand names	Cannabinoids they may contain
Spice, K2, Mojo, Aroma, Dream, Chill, Chaos, Sence, Smoke, Skunk, Space Diamond, Silent Black, Genie, Algerian Blend, Yucatan Fire, Tai Fun, Sensation, SpicyXXX, Spike 99, Bonsai-18, Banana Cream Nuke, Wicked X, Natures Organic, Zen	• JWH-018, JWH-019, JWH-073, JWH-167, JWH-250, JWH-253, JWH-387, JWH-398 • CP-47,497; cannabicyclohexanol • HU-210, HU-211 • AM-694

established (*Table 1*).[1-7,11-19,21-25] Current evidence supports that cannabis is a "component cause" of chronic psychosis, meaning although neither necessary nor sufficient, cannabis use at a young age increases the likelihood of developing schizophrenia or other psychotic disorders.[26] This risk may be greatest for young persons with some psychosis vulnerability (eg, those with attenuated psychotic symptoms).[16,18]

The overall magnitude of risk appears to be modest, and cannabis use is only 1 of myriad factors that increase the risk of psychosis.[27] Furthermore, most cannabis users do not develop psychosis. However, the risk associated with cannabis occurs during a vulnerable time of development and is modifiable. Based on conservative estimates, 8% of emergent schizophrenia cases and 14% of more broadly defined emergent psychosis cases could be prevented if it were possible to eliminate cannabis use among young people.[11,26] Therefore, reducing cannabis use among young people vulnerable to psychosis should be a clinical and public health priority.

Medical marijuana

Although cannabis extracts were marketed by major pharmaceutical companies and widely used by consumers for various ailments during the late 1800s, medicinal cannabis use in the United States declined significantly during the early 20th century. In 1937, the Marihuana Tax Act was passed, effectively putting a stop to physicians prescribing cannabis for medical purposes. The FDA currently classifies cannabis as a Schedule I drug (eg, high abuse potential, no currently accepted medical use, lack of safety data) and the use of cannabis and its prescription by physicians are prohibited under federal law.

However, in recognition of the potential medical benefits of cannabis, 16 states have legalized medicinal use ("medical marijuana") over the past several years. Laws and regulations governing medical marijuana vary from state to state. For example, in California, adults who obtain a recommendation from a physician and register for a Medical Marijuana Identification Card can legally purchase cannabis from a state-recognized dispensary and use it in a non-public setting. The physician's "recommendation" (not a prescription) is based upon the determination that "the person's health would benefit from the use of marijuana in the treatment of cancer, anorexia, AIDS, chronic pain, spasticity, glaucoma, arthritis, migraine, or *any other illness for which marijuana provides relief*"[28] (emphasis added). Although no state has yet legalized cannabis use for recreational purposes, with such regulations, an increasing number of jurisdictions have provided a way for consumers to easily obtain marijuana for loosely defined medical purposes.

Medical marijuana dispensaries offer a variety of cannabis strains, each with a different advertised "high" based upon variable proportions of Δ-9-THC and other constituents. The Δ-9-THC content of medical marijuana is about twice that of "street" marijuana, even with the latter's Δ-9-THC content rising to >10% over the past 15 years.[29,30] Therefore, medical marijuana is not only legal, but generally offers a more potent Δ-9-THC dose than typical street marijuana.

continued on page 55

Clinical Point

The magnitude of psychosis risk tied to cannabis use is modest and most users do not develop psychosis

continued from page 51

Table 3

Case reports of psychosis associated with synthetic cannabinoids

Study	N (age)	Herbal product or suspected cannabinoid	Previous psychotic disorder	Symptoms
Müller et al, 2010[a]	1 (25)	JWH-018 "Spice"	Yes	Anxiety, exacerbation of paranoid delusions, delusions of control, auditory hallucinations
Veamier et al, 2010[b]	1 (17)	JWH-018	No	Tachycardia, hypokalemia, agitation, visual hallucinations
Every-Palmer, 2010[c]	5	JWH-018 CP-47,497	Yes	Agitation, disorganization, paranoid and grandiose delusions
Rodgman et al, 2011[d]	3	JWH-018 ("Mojo")	—	"Mojo psychosis"
Benford et al, 2011[e]	1 (20)	JWH-018 ("Spice")	—	Tachycardia, anxiety, paranoia, auditory and visual hallucinations
Van Der Veer et al, 2011[f]	3 (20 to 30)	"Spice" "Spike 99"	No	Anxiety, disorganization, paranoia, Capgras delusion
Every-Palmer, 2011[g]	9 (20s to 40s)	JWH-018 ("Aroma")	Yes	Anxiety, agitation, paranoia
Hurst et al, 2011[h]	10 (21 to 25)	"Spice"	No	Anxiety, agitation, confusion, disorganization, paranoia, ideas of reference, hallucinations

Source: For reference citations, see this article at CurrentPsychiatry.com

A single case of psychosis emerging in the context of medical marijuana has been reported in the literature.[31] A 24-year-old man with mild, transient psychotic symptoms switched from street cannabis to medical marijuana for its superior potency and to conform with the law. He obtained a physician's recommendation based on diagnoses of "posttraumatic stress disorder" and "pain." After several months of increasingly frequent medical marijuana use, he developed florid and persistent psychotic symptoms necessitating antipsychotic medication, and was diagnosed with schizophrenia.

Although causality cannot be established based on this report, taken together with evidence that higher-potency cannabis is associated with a greater risk of psychotic emergence,[32] this case raises concerns about the iatrogenic and psychotoxic liability of medical marijuana use among those vulnerable to psychosis. Policy decisions about medical marijuana and its use among patients with psychiatric illness must be informed by evidence of its psychotic potential.

Synthetic cannabinoids

Synthetic cannabinoids were developed in the 1960s for research purposes and potential clinical applications, but have not been FDA-approved for therapeutic use.[33] Over the past 5 years, however, a variety of "herbal incense" products bearing names such as "Spice," "K2," and "Aroma" have emerged in Europe and the United States that contain botanicals laced with synthetic cannabinoids (*Table 2, page 51*).

Although herbal incense products are labeled "not for human consumption," they are sold by "head shops" and on the Internet without age restrictions and typically are purchased for the sole purpose of ingesting them, usually by smoking. Their desired effects resemble cannabis intoxication, including sedation, relaxation, altered consciousness, and euphoria. The products initially had the added appeal of being legal and undetectable in routine drug screening. Although not listed among the product's ingredients, chemical analyses confirmed these products typically contained 1 of 3 families of synthetic can-

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Clinical Point

Medical marijuana generally offers a more potent Δ-9-THC dose than typical illicit marijuana

Cannabis and psychosis

Related Resources

- Murray RM, Morrison PD, Henquet C, et al. Cannabis, the mind and society: the hash realities. Nat Rev Neurosci. 2007;8(11):885-895.
- European Monitoring Centre for Drugs and Drug Addiction: Synthetic cannabinoids and "spice." www.emcdda.europa.eu/publications/drug-profiles/synthetic-cannabinoids.
- U.S. Department of Justice, Drug Enforcement Agency, Office of Diversion Control: Schedules of controlled substances: temporary placement of five synthetic cannabinoids into Schedule I. www.deadiversion.usdoj.gov/fed_regs/rules/2011/fr0301.htm.

Disclosure

The author reports no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

Clinical Point

Case reports have linked use of herbal incense products containing synthetic cannabinoids to psychosis

nabinoid1 and cannabinoid2 (CB1/CB2) receptor agonists, designated by the prefixes JWH-, CP-, and HU-.[34] The compounds most commonly found in these analyses (JWH-018; CP-47,497; HU-210) have significantly greater potency (ie, CB1 receptor affinity) compared with Δ-9-THC.[33,34]

The growing popularity of herbal incense products has prompted health concerns based on reports of emergency presentations for adverse effects, including tachycardia, agitation, excess sedation, and loss of consciousness.[33,35,36] In addition, 8 anecdotal reports of psychosis associated with herbal incense (with a total of 33 patients) have emerged since 2010 (***Table 3, page 55***). Among them, a variety of psychotic symptoms are described in patients ranging in age from adolescence to adulthood, both with and without histories of psychosis. For those without a pre-existing psychotic disorder, symptoms were typically self-limited.

In the most recently presented case series of patients without pre-existing psychosis (N = 10), symptoms resolved in 70% of patients within 8 days, but 30% had psychosis that persisted beyond 5-month follow-up.[37] Collectively, these reports suggest that synthetic cannabinoid intoxication is associated with acute psychosis as well as exacerbations of previously stable psychotic disorders, and also may have a propensity to trigger a chronic psychotic disorder among vulnerable individuals.

Because of health concerns and the abuse potential of herbal incense products, many have been banned in several European countries, 18 U.S. states, and the U.S. military.[33,38] In March 2011, the FDA placed 5 synthetic cannabinoids (JWH-018, JWH-073, JWH-200, CP-47,497, and cannabicyclohexanol) on Schedule I, making them illegal to possess or sell in the United States.[38] However, there are hundreds of synthetic cannabinoid homologues, and herbal incense manufacturers have rapidly adapted by substituting other synthetic cannabinoids not yet banned by existing legislation.[34] The effects of these newly arising compounds in humans, including their psychotic potential, are largely unknown.

References

1. Degenhardt L, Tennant C, Gilmour S, et al. The temporal dynamics of relationships between cannabis, psychosis and depression among young adults with psychotic disorders: findings from a 10-month prospective study. Psychol Med. 2007;37(7):927-934.
2. Zammit S, Moore TH, Lingford-Hughes A, et al. Effects of cannabis use on outcomes of psychotic disorders: systematic review. Br J Psychiatry. 2008;193(5):357-363.
3. Zuardi AW, Crippa JA, Hallak JE, et al. Cannabidiol, a Cannabis sativa constituent, as an antipsychotic drug. Braz J Med Biol Res. 2006;39(4):421-429.
4. Zuardi AW, Hallak JE, Dursun SM, et al. Cannabidiol monotherapy for treatment-resistant schizophrenia. J Psychopharmacol. 2006;20(5):683-686.
5. Morgan CJ, Curran HV. Effects of cannabidiol on schizophrenia-like symptoms in people who use cannabis. Br J Psychiatry. 2008;192(4):306-307.
6. Schwarcz G, Karajgi B, McCarthy R. Synthetic delta-9-tetrahydrocannabinol (dronabinol) can improve the symptoms of schizophrenia. J Clin Psychopharmacol. 2009;29(3):255-258.
7. Schwarcz G, Karajgi B. Improvement in refractory psychosis with dronabinol: four case reports. J Clin Psychiatry. 2010;71(11):1552-1553.
8. D'Souza DC, Perry E, MacDougall L, et al. The psychotomimetic effects of intravenous delta-9-tetrahydrocannabinol in healthy individuals: implications for psychosis. Neuropsychopharmacology. 2004;29(8):1558-1572.
9. Morrison PD, Zois V, McKeown DA, et al. The acute effects of synthetic intravenous Delta9-tetrahydrocannabinol on psychosis, mood and cognitive functioning. Psychol Med. 2009;39(10):1607-1616.
10. Favrat B, Ménétrey A, Augsburger M, et al. Two cases of "cannabis acute psychosis" following the administration of oral cannabis. BMC Psychiatry. 2005;5:17.
11. Moore TH, Zammit S, Lingford-Hughes A, et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. Lancet. 2007;370(9584):319-328.
12. Minozzi S, Davoli M, Bargagli AM, et al. An overview of systematic reviews on cannabis and psychosis: discussing apparently conflicting results. Drug Alcohol Rev. 2010;29(3):304-317.
13. Andréasson S, Allebeck P, Engström A, et al. Cannabis and schizophrenia. A longitudinal study of Swedish conscripts. Lancet. 1987;2(8574):1483-1486.
14. Zammit S, Allebeck P, Andreasson S, et al. Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: historical cohort study. BMJ. 2002;325(7374):1199.

15. Arseneault L, Cannon M, Poulton R, et al. Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. BMJ. 2002;325(7374):1212-1213.
16. van Os J, Bak M, Hanssen M, et al. Cannabis use and psychosis: a longitudinal population-based study. Am J Epidemiol. 2002;156(4):319-327.
17. Fergusson DM, Horwood LJ, Swain-Campbell NR. Cannabis dependence and psychotic symptoms in young people. Psychol Med. 2003;33(1):15-21.
18. Henquet C, Krabbendam L, Spauwen J, et al. Prospective cohort study of cannabis use, predisposition for psychosis, and psychotic symptoms in young people. BMJ. 2005; 330(7481):11.
19. Kuepper R, van Os J, Lieb R, et al. Continued cannabis use and risk of incidence and persistence of psychotic symptoms: 10 year follow-up cohort study. BMJ. 2011;342:d738.
20. Henquet C, Murray R, Linszen D, et al. The environment and schizophrenia: the role of cannabis use. Schizophr Bull. 2005;31(3):608-612.
21. Semple DM, McIntosh AM, Lawrie SM. Cannabis as a risk factor for psychosis: systematic review. J Psychopharmacol. 2005;19(2):187-194.
22. D'Souza DC, Abi-Saab WM, Madonick S, et al. Delta-9-tetrahydrocannabinol effects in schizophrenia: implications for cognition, psychosis, and addiction. Biol Psychiatry. 2005;57(6):594-608.
23. Large M, Sharma S, Compton MT, et al. Cannabis use and earlier onset of psychosis: a systematic meta-analysis. Arch Gen Psychiatry. 2011;68(6):555-561.
24. Kristensen K, Cadenhead KS. Cannabis abuse and risk for psychosis in a prodromal sample. Psychiatry Res. 2007;151(1-2):151-154.
25. Phillips LJ, Curry C, Yung AR, et al. Cannabis use is not associated with the development of psychosis in an "ultra" high-risk group. Aust N Z J Psychiatry. 2002;36(6):800-806.
26. Arseneault L, Cannon M, Witton J, et al. Causal association between cannabis and psychosis: examination of the evidence. Br J Psychiatry. 2004;184:110-117.
27. Tandon R, Keshavan MS, Nasrallah HA. Schizophrenia, "just the facts" what we know in 2008. 2. Epidemiology and etiology. Schizophr Res. 2008;102(1-3):1-18.
28. California Secretary of State. California Proposition 215: Text of proposed law. Available at: http://vote96.sos.ca.gov/Vote96/html/BP/215text.htm. Accessed July 27, 2011.
29. Burgdorf JR, Kilmer B, Pacula RL. Heterogeneity in the composition of marijuana seized in California. Drug Alcohol Depend. 2011;117(1):59-61.
30. Gieringer D. Medical cannabis potency testing project. Bulletin of the Multidisciplinary Association for Psychedelic Studies. 1999;9(3):20-22. Available at: http://www.maps.org/news-letters/v09n3/09320gie.html. Accessed July 27, 2011.
31. Pierre JM. Psychosis associated with medical marijuana: risk vs. benefits of medicinal cannabis use. Am J Psychiatry. 2010;167(5):598-599.
32. Di Forti M, Morgan C, Dazzan P, et al. High-potency cannabis and the risk of psychosis. Br J Psychiatry. 2009; 195(6):488-491.
33. Vardakou I, Pistos C, Spiliopoulou CH. Spice drugs as a new trend: mode of action, identification and legislation. Toxicol Lett. 2010;197(3):157-162.
34. Dresen S, Ferreirós N, Pilitz M, et al. Monitoring of herbal mixtures potentially containing synthetic cannabinoids as psychoactive compounds. J Mass Spectrom. 2010; 45(10):1186-1194.
35. Simmons JR, Skinner CG, Williams J, et al. Intoxication from smoking "spice." Ann Emerg Med. 2011;57(2):187-188.
36. Schneir AB, Cullen J, Ly BT. "Spice" girls: synthetic cannabinoid intoxication. J Emerg Med. 2011;40(3): 296-299.
37. Hurst D, Loeffler G, McLay R. Synthetic cannabinoid agonist induced psychosis: a case series. Presented at: 164th Annual Meeting of the American Psychiatric Association; May 14-18, 2011; Honolulu, HI.
38. U.S. Department of Justice Drug Enforcement Agency. Temporary placement of five synthetic cannabinoids into schedule I. Available at: http://www.deadiversion.usdoj.gov/fed_regs/rules/2011/fr0301.htm. Accessed July 27, 2011.

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Clinical Point

The FDA has placed 5 synthetic cannabinoids on Schedule I, but there are hundreds of synthetic cannabinoid homologues

Bottom Line

Evidence has consistently demonstrated that cannabis use is a risk factor for psychosis, both for those with existing psychotic disorders and for young people vulnerable to psychosis. Clinicians must be aware of the psychotic potential of cannabis and synthetic cannabinoids, monitor for psychotic emergence among users, and take care not to neglect cannabis use disorders when planning treatment.

Table 3

Case reports of psychosis associated with synthetic cannabinoids

References

a. Müller H, Sparling W, Köhrmann M, at al. The synthatic cannabinoid Spice as a triggar for an acuta axacerbation of cannabis induced recurrent psychotic episodes. Schizophr Res. 2010;118(1-3):309-310.

b. Vearrier D, Osterhoudt KC. A teenagar with agitation: higher than she should hava climbed. Pediatr Emarg Care. 2010;26(6):462-465.

c. Every-Palmer S. Warning: legal synthatic cannabinoid-recaptor agonists such as JWH-018 may praclpitate psychosis in vulnarable individuals. Addiction. 2010;105(10):1859-1860.

d. Rodgman C, Kinzie E, Leimbach E. Bad Mojo: use of tha naw marijuana substituta laads to more and more ED visits for acute psychosis. Am J Emerg Med. 2011;29(2):232.

a. Benford DM, Caplan JP. Psychiatric saquelae of spice, K2, and synthetic cannabinoid receptor agonists. Psychosomatics. 2011;52(3):295.

f. Van Der Veer N, Friday J. Persistent psychosis following the usa of Spice. Schizophr Res. 2011;130(1-3):265-266.

g. Every-Palmer S. Synthatic cannabinoid JWH-018 and psychosis: an explorativa study. Drug Alcohol Depand. 2011. [Epub ahead of print].

h. Hurst D, Loeffler G, McLay R. Synthatic cannabinoid agonist induced psychosis: a case series. Presented at: 164th Annual Meating of the American Psychiatric Association; May 14-18, 2011; Honolulu, HI.

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Exhibit 3

Scientifically Unfounded Claims in Diagnosing and Treating Patients

To the Editor: We greatly appreciated the thoughtful book review by Andrew F. Leuchter, M.D. (1), published in the May 2009 issue of the *Journal*, on Daniel Amen's *Healing the Hardware of the Soul: Enhance Your Brain to Improve Your Work, Love, and Spiritual Life* (2). Dr. Amen claims that numerous psychiatric illnesses can be diagnosed and treatments prescribed based on resting single photon emission computerized tomography (SPECT) images. Dr. Leuchter correctly points out the absence of empirical data to support the claims of Dr. Amen. Several years ago, following conversations with Dr. Amen on how to address such concerns, the Brain Imaging Council of the Society of Nuclear Medicine offered Dr. Amen the opportunity to submit his analyses of a blinded set of SPECT scans (to have been prepared by the Brain Imaging Council) to determine how effective his technique is at correctly diagnosing subjects. Although this proposed study could have provided support for his approach, the offer was declined. Nevertheless, for more than two decades, Dr. Amen has persisted in using scientifically unfounded claims to diagnose and treat patients (over 45,000 by his own count).

There are several dangers to patients that can accrue from this approach: 1) patients (including children) are administered a radioactive isotope without sound clinical rationale; 2) patients pursue treatments contingent upon an interpretation of a SPECT image that lacks empirical support; and 3) based on a presumed diagnosis provided by Dr. Amen's clinics, patients are guided toward treatment that may detract them from clinically sound treatments.

Just as serious is the danger to our field. It is likely that, within the next decade, Dr. Amen's claims will be realized in that psychiatrists will enjoy the ability to diagnose and prescribe treatments based, in part, upon neuroimaging findings. Unfortunately, if previously led astray by unsupported claims, patients and their doctors may be less inclined to utilize scientifically proven approacbes once these are sbown in the peer-reviewed literature to be effective.

It is therefore incumbent upon all of us to monitor and regulate our field. We encourage physicians to remain vigilant of unproven approaches practiced by our peers and to immediately report these trespasses to their state medical boards.

References

1. Leuchter AF: Healing the hardware of the soul: enhance your brain to improve your work, love, and spiritual life, by Daniel Amen (book review). Am J Psychiatry 2009; 166:625
2. Amen D: Healing the Hardware of the Soul: Enhance Your Brain to Improve Your Work, Love, and Spiritual Life. New York, Simon and Schuster, 2008

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Dr. Adinoff has received grant/research support from the Department of Veterans Affairs, the National Institute on Alcohol Abuse and Alcoholism, and the National Institute on Drug Abuse; he has served as a consultant to GlaxoSmithKline, the Hershewe Law Firm, Phillips Lytle (for GlaxoSmithKline), Shook, Hardy and Bacon, Simon Pissante, and Teva Pharmaceutical Industries; and he has received honoraria from the American Academy of Addiction Psychiatry, the Medical University of South Carolina, and the University of New Mexico. Dr. Devous has received research support from Alseres and AVID Radiopharmaceuticals, and he has served on the scientific advisory board of AVID Radiopharmaceuticals.

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Psychosis Associated With Medical Marijuana: Risk vs. Benefits of Medicinal Cannabis Use

To the Editor: Over the past 15 years, it bas become increasingly evident that cannabis use carries an increased risk for the development of psycbosis (1, 2). At the same time, medicinal cannabis (medical marijuana) has been legalized in many states, with minimal restrictions on prescribing indications. Tbe present case illustrates the evolution of a psychotic disorder, in the setting of medicinal cannabis use, in a young man at high risk for psychosis.

"Mr. Z" was a 24-year-old man who was first hospitalized for insomnia, irritability, and aggressiveness 2 years after military service. On admission, he displayed heightened religiosity and mild suspiciousness. Urine toxicology screening revealed cannabinoids, supporting the patient's endorsed semi-daily cannabis use via water pipe for the past 18 months, without other substance abuse. He was started on quetiapine (100 mg/day), with rapid resolution of symptoms, and discharged after 10 days.

The patient subsequently discontinued quetiapine and was lost to follow-up. Four months later, he presented to a marijuana clinic complaining of chronic pain, insomnia, and anxiety and was given a diagnosis of posttraumatic stress disorder (PTSD) and pain, along with a medical recommendation for cannabis. No psychotic symptoms were elicited. He later explained that he switched from "street" marijuana to medical marijuana in order to obtain a more potent product as well as to avoid illegal activity and getting "ripped off" by drug dealers. He also increased the frequency of his daily use from approximately once to twice daily.

Six months later, Mr. Z was rehospitalized with new-onset auditory hallucinations (multiple voices speaking to each other and urging violence) and delusions (believing that people were tampering with his windows and eavesdropping on his conversations and that he was Jesus Christ). Aripiprazole (15 mg/day) was prescribed, with gradual symptomatic improvement, and then tapered to a lower dose (7.5 mg/day) due to tremor. The patient reported that he believed smoking cannabis helped his chronic pain but that it worsened his psychotic symptoms, such that he wanted help to stop smoking the drug. After 4 weeks, he was discharged to residential substance abuse treatment with only mild, residual psychotic symptoms and a discharge diagnosis of psychotic disorder not otherwise specified, PTSD, and cannabis dependence. At a 3-month follow-up evaluation, while still taking aripiprazole, Mr. Z remained off cannabis and free of psychotic symptoms.

Although cannabis may have some bealth benefits, it also has a variety of adverse effects, including psychosis, especially among those at high risk (1–3). The patient in the present case was at high risk for psycbosis based on attenuated symp-

toms at first presentation, with evolution of frank psychosis potentially explained by his increased use of cannabis and the greater potency of medicinal relative to "street" cannabis (4). This case underscores the importance of 1) aggressively managing cannabis use in patients at high risk for psychosis and those already suffering from psychosis, 2) apprising physicians who prescribe/recommend medicinal cannabis of its iatrogenic and psychototoxic liability among sucb individuals, 3) educating the public about the risk of cannabis-induced psychosis, and 4) the need for recent evidence about this public health risk to inform policy decisions about medicinal cannabis in the United States (3).

References

1. Moore THM, Zammit S, Lingford-Hughes A, Barnes TRE, Jones PB, Burke M, Lewis G: Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. Lancet 2007; 370:319–328
2. Compton MT, Kelley ME, Ramsay CE, Pringle M, Goulding SM, Esterberg ML, Stewart T, Walker EF: Association of pre-onset cannabis, alcohol, and tobacco use with age at onset of prodrome and age at onset of psychosis in first-episode patients. Am J Psychiatry 2009; 166:1251–1257
3. Hall W: The adverse health effects of cannabis use: What are they, and what are their implications for policy? Int J Drug Policy 2009; 20:458–466
4. Di Forti M, Morgan C, Dazzan P, Pariante C, Modelli V, Marques TR, Hadley R, Luzi S, Russo M, Paparelli A, Butt A, Stilo SA, Wiffen B, Powell J, Murray RM: High-potency cannabis and the risk of psychosis. Br J Psychiatry 2009; 195:488–491

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Do Antidepressants Alter Emotional Processing in PTSD?

To the Editor: I read with interest the article by Catherine J. Harmer, D. Phil., et al. (1), published in the October 2009 issue of the *Journal*, on the effects of antidepressants on negative affective bias in depressed patients. The authors raised the possibility that antldepressants exert effects by altering emotional processing early in treatment. They also noted that their results are consistent with cognitive theories of depression.

The study's findings remind me of the effects of selective serotonin reuptake inhibitors (SSRIs) on anger, which I have observed in patients with combat-related posttraumatic stress disorder (PTSD). I've noted that treatment with SSRIs often produces a discernible reduction in observed and internally experienced anger preceding any reduction in other PTSD symptoms or depression. Patients report that their "fuse" seems longer and that they see things that used to make them angry but somehow do not bother them as much. This reduced inclination toward anger frequently occurs within a few days of starting treatment and sometimes occurs at lower than usual doses, consistent with the lower dosing of reboxetine conducted by Harmer et al. Sometimes it is the patient's spouse, not the patient, who first notices that the patient seems less angry. Sometimes the ameliorative effect of SSRIs on anger is reaffirmed with medication discontinuation. I have had spouses correctly suspect that their husband was secretly medication noncompliant based on their perception of his increased anger. One patient, a former Vietnam medic, was able to articulate a change in his perceptions with sertraline discontinuation. Within days, he perceived that people around him were suddenly "lots more angry and difficult." He realized, of course, that this was unlikely and that it was his appraisal of others that had suddenly changed.

Tbese clinical experiences suggest that SSRIs may alter emotional processing in PTSD patients not unlike that seen with reboxetine in depressed patients. (1) Although there are potential alternative explanations for the aforementioned clinical observations (e.g., improvements in anger in PTSD patients may be one aspect of a general SSRI-induced emotional dampening [2] and improvement in anger might be a manifestation of a global improvement in PTSD), the timing of the improvements (i.e., early in treatment) and the reports of altered perception of external events are reminiscent of Harmer et. al's findings. It may be that changes in emotional processing by antidepressants play a role in the treatment of PTSD just as they appear to do in depression.

References

1. Harmer CJ, O'Sullivan U, Favaron E, Massey-Chase R, Ayres R, Reinecke A, Goodwin GM, Cowen PJ: Effect of acute antidepressant administration on negative affective bias in depressed patients. Am J Psychiatry 2009; 166:1178–1184
2. Price J, Cole V, Goodwin GM: Emotional side-effects of selective serotonin reuptake inhibitors: qualitative study. Br J Psychiatry 2009; 195:211–217

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The author reports no financial relationships with commercial interests.

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Drs. Harmer, Goodwin, and Cowen Reply

To the Editor: We thank Dr. Hierholzer for his interest in our hypothesis that antidepressant drug treatments have early effects on the evaluation of emotional material, whicb are important in the development of clinical mood change over time (1). We agree that this hypothesis of antidepressant drug action may also extend to anxiety disorders. In his clinical observations, he suggests that anger is reduced early on with SSRI treatment in PTSD. These clinical observations are consistent with an earlier study (2), whicb found a decrease in anger recognition following 7 days of administration of the SSRI citalopram in bealthy volunteers. It is encouraging that these findings in healthy people in a laboratory setting may translate into a different patient group and to a real-world setting. Consistent with these findings, Davidson et al. (3) reported that early effects on anger and irritability were predictive of therapeutic response to sertraline in individuals with PTSD.

To test Dr. Hierholzer's clinical observations using a cognitive psychology approach, it will be important to observe whether behavioral and neural biases toward anger-related

THE UNIVERSITY OF ARIZONA | MEL AND ENID ZUCKERMAN COLLEGE OF PUBLIC HEALTH

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Medical Marijuana for the Treatment of Post Traumatic Stress Disorder:

An Evidence Review

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Introduction

Purpose of evidence review

This review evaluates evidence on cannabis use in adults for the treatment of post-traumatic stress disorder (PTSD). The Arizona Department of Health Services (ADHS), which funded this report, to assist in assessing PTSD as a condition to add to those that qualify for the use of medical marijuana in Arizona.

Background

Pursuant to A.R.S. § 36-2801.01, the puhlic may petition the Arizona Department of Health Services (ADHS) to add debilitating medical conditions to those listed in A.R.S. 36-2801(3). The ADHS estahlished the manner in which it shall consider petitions to add dehilitating medical conditions in A.A.C. R9-17-106. A.A.C. R9-17-106(C) states, ADHS "shall accept requests for the addition of a medical condition to the list of debilitating medical conditions in R9-17-201 in January and July of each calendar year starting in January 2012". After receiving requests for adding conditions the ADHS requests a report on the scientific evidence on the use of cannahis for this condition from the University of Arizona College of Public Health. In addition the Department holds a public hearing to hear puhlic testimony on the condition and its treatment with cannabis. The Department Medical Advisory Committee then considers the totality of the evidence in deciding to add a condition to the list, or not.

Scope of evidence review

List of Key Questions

Benefits and harms of cannahis therapy for PTSD

1. What are the benefits (short and long-term henefits) of cannahis use for those with post-traumatic stress disorder?
2. What are the harms (short and long-term harms) of cannabis use for post-traumatic stress disorder patients?
3. What are the henefits and harms of cannabis for treating post traumatic stress disorder in patients with a history of substance abuse or addiction that are undergoing treatment for addiction?

Conflict of Interest

None of the reviewers conducting this review have any conflicts of interest to disclose.

Methods

Dates of Search

March 2012 – June 2012

Population

Adults (≥ 18 years old)

Literature search and strategy

The topics of cannabis use and post-traumatic stress disorder where searched in the following databases: The Cochrane Library, Ovid MEDLINE® and PsycINFO. Bibliographies of articles identified through databases were hand searched for pertinent articles. In addition, there was a gray literature search using Google Scholar to identify electronically published articles and current unpublished studies. A detailed description of each search can be found in Appendix 1.

Inclusion and exclusion criteria

All identified studies were imported into an electronic database (RefWorks) and considered for inclusion. We included studies that met all of the following criteria:

1. Evaluated adults (≥ 18 years old) with post traumatic stress disorder
2. English language
3. Human study
4. Were relevant to one of the Key Questions

Excluded articles included those that were: animal studies, or experiments on biochemical or pathophysiological pathways; case reports or case series; editorials or opinions; not addressing a key question.

Data synthesis

Observational studies were assessed using the main domains described in tools commonly used (Deeks JJ, Dinnes J, D'Amico R, Sowden AJ, Sakarovitch C, Song F, et al. Evaluating non-randomized intervention studies. Health Technology Assessment 2003;7(27)). The overall quality of the evidence is ranked using GRADE methodology demonstrated in Appendix 2. (Owens DK, Lohr KN, Atkins D, et al. Grading the strength of a body of evidence when comparing medical interventions. In: Agency for Healthcare Research and Quality. Methods Guide for Comparative Effectiveness Reviews. Rockville, MD. Available at: http://effectivehealthcare.ahrq.gov/healthInfo.cfm?infotype=rr&ProcessID=60.).

Results

Findings

A total of 48 articles were identified through The Cochrane Library, PubMed and PsychINFO and another 6 were discovered from references cited in key articles. No study was found that focused on the treatment effects of cannabis on those with PTSD. The table below lists the 18 article that came the closest to addressing any of the key questions. Those bolded are the highest quality with the most pertinent findings.

The entire list of articles is included in Appendix 3.

Article , Citation and Database	Description and Design of Study	Limitations	Quality
1. Bonn-Miller MO, Vujanovic AA, Boden MT,	The study tested whether the	The study was about the	Very low quality - The study's

Gross JJ. Posttraumatic stress, difficulties in emotion regulation, and coping-oriented marijuana use. Cogn Behav Ther. 2011 Mar;40(1):34-44. Database: PubMed & PsycINFO	association between posttraumatic stress symptom severity and marijuana use coping motives is mediated by difficulties in emotion regulation. Cross-sectional study (n=79) California	association of PTSD and marijuana use coping motives, not benefits or harms of marijuana. All subjects had both PTSD and marijuana use.	limitations include: recall bias and self selected sample. The design does not permit an examination of the temporal relations between PTSD severity, emotion regulation difficulties, and coping-oriented marijuana use. Small number of participants.
2. Bonn-Miller MD, Vujanovic AA, Drescher, Kent D. Cannabis use among military veterans after residential treatment for posttraumatic stress disorder. Psychol Addict Behav. 2011 September;23(3):485-91. Database: PsychINFO	**The study prospectively evaluated whether treatment changes in PTSD symptom severity, among Veterans in residential PTSD treatment, were related to cannabis use 4 months after discharge from residential rehabilitation. Prospective cohort (4 month, n= 432) Veterans in residential program for PTSD treatment at a VA centre.**	**Found that Veterans who experienced lower levels of change in PTSD symptom severity during the course of residential treatment for PTSD were more likely to use cannabis after discharge from treatment.**	**Low to moderate quality– The sample is self selected and demographically homogenous. There potential for bias (recall).**
3. Bonn-Miller MO, Vujanovic AA, Feldner MT, Bernstein A, Zvolensky MJ. Posttraumatic stress symptom severity predicts marijuana use coping motives among traumatic event-exposed marijuana users. J Trauma Stress. 2007 Aug;20(4):577-86. Database: PubMed & PsycINFO	The study examines the relation between posttraumatic stress symptom severity and motives for marijuana use. Cross-sectional study (n=103 young adults) Vermont	Posttraumatic stress symptom severity was significantly related to coping-oriented marijuana use motives.	Very low quality – The study is not generalizable as the sample was demographically homogenous, age-limited and self-selected. The participants had experienced relatively limited number of traumatic life events. There is large potential for bias (recall).
4. Bonn-Miller MO, Vujanovic AA, Twohig MP, Medina JL, Huggins JL. Posttraumatic stress symptom severity and marijuana use coping motives: A test of the mediating role of non-judgmental acceptance within a trauma-exposed community sample. Mindfulness. 2010 May;(1):98-106. Reference from Cougle, et al.	The study examined the role of non-judgmental acceptance in the relation between posttraumatic stress symptom severity and marijuana use coping motives. Cross-sectional study (n=97)	This study did not address the key questions as it was about the association of PTSD and marijuana use coping motives, not the benefits or harms of marijuana use.	Very low quality – The study had a non-generalizable sample and was limited by the high potential for bias (recall).
5. Bremner JD, Southwick SM, Darnell A, Charney DS. Chronic PTSD in vietnam combat veterans: Course of illness and substance abuse. Am J Psychiatry. 1996 Mar;153(3):369-75. Database: PubMed	The purpose of this study was to measure the longitudinal course of specific symptoms of posttraumatic stress disorder (PTSD) and related symptoms of alcohol and substance abuse and the effects of alcohol and substances on the symptoms of PTSD. Cross-sectional study (n=61) of Vietnam combat veterans , North East U S	This study is not intended to study the effects of marijuana on PTSD. The findings are that substance use of all kinds is associated with increased symptoms of PTSD and those who are using these substances (alcohol, heroine, cocaine and marijuana) report benefit.	Very low quality - The potential for recall bias is large, and the outcomes are not validated.
6. Chilcoat HD, Breslau N. Investigations of causal pathways between PTSD and drug use disorders. Addict Behav. 1998 Nov-Dec;23(6):827-40. Reference from Cougle, et al.	This study addressed the potential causal pathways between PTSD and substance use disorders. Cohort study (n=1007)	The study did not address the key questions.	Low quality – The sample had potential for bias as it was limited to one HMO, there was an underrepresentation of extremes of socioeconomic status, and participants were young adults aged 21-30 years of age.

7. Chilcoat HD, Breslau N. Posttraumatic stress disorder and drug disorders: Testing causal pathways. Arch Gen Psychiatry. 1998 Oct;55(10):913-7. Reference from Cougle, et al.	This article examined existing studies of PTSD and substance use and used epidemiological data from article #6 to demonstrate analytical strategies to best address the causal relationship between these disorders. Cohort study (n=1007 adults in Michigan) two follow ups at 3 and 5 years.	PTSD was a risk for drug abuse (OR 4.5) but was not significant for marijuana use.	Low to moderate quality – The sample had potential for bias as it was limited to one HMO, there was an underrepresentation of extremes of socioeconomic status, and participants were young adults aged 21-30 years of age.
8. Cornelius JR, Kirisci L, Reynolds M, Clark DB, Hayes J, Tarter R. PTSD contributes to teen and young adult cannabis use disorders. Addict Behav. 2010 Feb;35(2):91-4. **Database: PubMed & PsycINFO**	**This study addresses the effect of PTSD on CUD among teenagers transitioning to young adulthood.** **Longitudinal cohort study (n=693, 31 w/ PTSD) Subjects were sons of men with SUD. Recruited at ages 10-12 and seeu 5 times up to age 25.**	**The study did not address the key questions (no benefit or harm was studied). Of the 19 participants who met diagnostic criteria for both CUD and PTSD, 9 had PTSD first and CUD second, 9 had CUD first and PTSD second, and 1 had the onset of both diagnoses at the same age.**	**Moderate quality– Very small numbers with PTSD, large potential for bias in the sample selection. Large loss to follow up.**
9. Cougle JR, Bonn-Miller MO, Vujanovic AA, Zvolensky MJ, Hawkins KA. Posttraumatic stress disorder and cannabis use in a nationally representative sample. Psychol Addict Behav. 2011 Sep;25(3):554-8. **Database: PubMed & PsycINFO**	**The study examined the relationship between PTSD and cannabis use in a large representative survey of adults from the United States.** **Cross-sectional study (n=5672)**	**The study found an association between PTSD and marijuana use but could not assess benefits/harms or causation. Lifetime and current (past year) PTSD diagnoses were associated with increased odds of lifetime history of cannabis use as well as past year daily cannabis use. Odds ratios were in the 2-3 raoge.**	**Moderate to high quality– Quality upgrade because of representative sampling and large odds ratios found. The study controls for multiple other variables that could affect both PTSD and marijuana use.**
10. Johnson SD, Striley C, Cottler LB. The association of substance use disorders with trauma exposure and PTSD among african american drug users. Addict Behav. 2006 Nov;31(11):2063-73. Database: PubMed	This study examines the association of traumatic exposure, PTSD and substance use among 1098 out-of-treatment African American drug users. Cross-sectional design (n=1098)	The study did not address the benefit or harm of using cannabis. There were some associations found between traumatic events and alcohol and marijuana abuse but the odds ratios are small and confidence intervals wide.	Very low quality – Very limited sample (AA female drug abusers). There is also a large potential for bias (recall). The traumatic events were of multiple typew and may not actually be associated with ptsd.
11. Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the national comorbidity survey. Arch Gen Psychiatry. 1995 Dec;52(12):1048-60. Reference from Cougle, et al.	The investigation examined general population data from the national comorbidity survey. . Cross-sectional design (n=5877)	This article concluded that PTSD is more prevalent than previously believed. The lifetime prevalence of PTSD was found to be 7.8% (with an SE of 0.5%). The lifetime prevalence of trauma exposure was found to be 60.7% for men and 51.2% for women.	Low to moderate quality - The data came from the NCS, a survey designed to study the distribution, correlates, and consequences of psychiatric disorders in the United States. There is a high potential for recall bias. It does not address marijuana use
12. Potter CM, Vujanovic AA, Marshall-Berenz EC, Bernstein A, Bonn-Miller MO. Posttraumatic stress and marijuana use coping motives: The mediating role of distress	The investigation examined the explanatory role of distress tolerance in the relation between posttraumatic stress symptom	This study focuses on the motives behind marijuana use not the benefit or the harm of	Very low quality – Self selected sample, large potential for bias.

tolerance. J Anxiety Disord. 2011 Apr;25(3):437-43. Database: PsychINFO	severity and marijuana use coping motives. Cross-sectional design (n=142) adults in Vermont recruited in several ways, not well described.	marijuana use among PTSD patients. Found that trauma-exposed marijuana users with greater PTS symptom severity may use marijuana to cope with negative mood states, at least partially because of a lower percelved capacity to withstand emotional distress.	
13. Stewart SH, Conrod PJ, Pihl RO, & Dongier, M. Relations Between Posttraumatic Stress Symptom Dimensions and Substance Dependence in a Community-Recruited Sample of Substance-Abusing Women. Psychology of Addictive Behaviors. 1999. Vol. 13(2):78-88. Reference from Cougle, et al.	This study examined the factor structure of PTSD symptoms, and correlations between PTSD dimensions and substance dependence. Cross-sectional design (N=295) substance abusing women	This study discussed the association of marijuana use and PTSD (no benefit/harm was discussed).	Very low quality –This was a nonrandom sample and there is a large potential for blas.
14. Villagonzalo KA, Dodd S, Ng F, Mihaly S, Langbein A, 8erk M. The relationship between substance use and posttraumatic stress disorder in a methadone maintenance treatment program. Compr Psychiatry. 2011 Sep-Oct;52(5):562-6. Database: PubMed	This study explores the relationship between substance abuse and PTSD symptom clusters in a methadone maintenance population in Australia. Cross-sectional (n=80)	This article discusses the self medication hypothesis but does not address whether cannabis use is harmful or beneficial to the PTSD population. Severity of marijuana use was significantly associated with a number of re experiencing and hyperarousal symptoms and with overall severity of PTSD symptoms. Opiate, amphetamine, and benzodiazepine use did not appear to be related to PTSD symptoms.	Very low quality– This Is a nonrandom sample with a large non-particlpation rate and with large potential for bias (recall).
15. Vlahov D, Galea S, Ahern J, Resnick H, Boscarino JA, Gold J, et al. Consumption of cigarettes, alcohol, and marijuana among new york city residents six months after the september 11 terrorist attacks. Am J Drug Alcohol Abuse. 2004 May;30(2):385-407. Database: PubMed	Random-digit phone survey was conducted to estimate the prevalence of increased substance use among residents of New York City six to nine months after the attacks. Cross-sectional design (n=1,570)	This study does not speak to the benefit or harm of cannabis use among PTSD population. Many of those interviewed did not have PTSD. Doruments a 2.7% increae in marijuana use following 9-11.	Very low quality – Self reported drug use. Large potential for bias.
16. Vlahov D, Galea S, Resnick H, Ahern J, Boscarino JA, Bucuvalas M, et al. Increased use of cigarettes, alcohol, and marijuana among manhattan, new york, residents after the september 11th terrorist attacks. Am J Epidemiol. 2002 Jun 1;155(11):988-96. Database: PubMed	A random-digit dial telephone survey was conducted to estimate the prevalence of increased cigarette smoking, alcohol consumption, and marijuana use among residents of Manhattan, Ney York City, 5-8 weeks after the attacks. Cross-sectional design (n=988) New York City Following 9-11	This study does not address the benefit or harm of cannabis use among PTSD population. Documents a 3,2 % increase in marijuana use following 9-11	Very low quality– No validation of reported drug use.
17. Xian H, Scherrer JF, Grant JD, Eisen SA, True WR, Jacob T, et al. Genetic and environmental contributions to nicotine, alcohol and cannabis dependence in male	This study aims to compute the common and specific genetic environmental contribution to nicotine dependence, alcohol	This article does not address the benefit or harm cannabis use has on PTSD population. It	Low to moderate quality– This study is not generalizable. The sample included only male twins. The use of cannabis among the

twins. Addiction. 2008 Aug;103(8):1391-8. Database: PubMed	dependence and cannabis dependence. Longitudinal cohort design (n=1498 dyzygotic twins, 1874 monzygotic twins born between 1939-1975 both twins in military service)	demonstrates that both genetic and environmental factors influence cannabis dependency, but the analysis is difficult to follow.	sample was low. The statistical analysis is hard to follow.
18. Kilpatrick DG, Acierno R, Saunders B et al. Risk factors for adolescent substance abuse and dependence: data from a national sample.	**Cross sectional study. National sample of 4023 adolescents ages 12-17, using telephone survey.**	**PTSD independently increased risk of marijuana and hard drug use disorders but not alcohol abuse/dependence.**	**Low to moderate quality. National sample, recall bias potential, confounders controlled for.**

Summaries

Summary of gray literature

There were no studies identified that researched the benefits or harms of cannabis use among the PTSD population. Many articles recommend further research and evaluation of the co-occurrence of PTSD and cannabis use.

Summary of articles provided with public petition to ADHS

The three articles provided by the public are summarized in the table below.

Article and Database	Description and Design of Study	Exclusion Reasoning	Quality
1. Ashton CH. Pharmacology and effects of cannabis: A brief review. Br J Psychol. 2001;178:101-6.	The aim of the study is to highlight recent knowledge of mechanisms of action, effects on psychomotor and cognitive performance, and health risks associated with cannabis consumption.	This article does not discuss PTSD.	Not quantifiable – This article is a brief review of recent literature on the prevalence of recreational cannabis use, the potency of modern cannabis preparations and the pharmacological actions of cannabis.
2. Crean RD, Crane NA, Mason BJ. An evidence based review of acute and long-term effects of cannabis use on executive cognitive functions. J Addict Med. 2011 Mar;5(1):1-8.	This is a review of the research on the acute, residual, and long-term effects of cannabis use on executive functions and discusses the implications for treatment.	This article does not discuss PTSD.	This study is an evidence-based review but does not address PTSD.
3. Solowij N, Stephens RS, Roffman RA, Babor T, Kadden R, Miller M, et al. Cognitive functioning of long-term heavy cannabis users seeking treatment. JAMA. 2002 Mar 6;287(9):1123-31.	The objective of this study is to examine the effects of duration of cannabis use on specific areas of cognitive functioning among users seeking treatment for cannabis dependence. Cross-sectional Design (n=102)	This article does not discuss PTSD.	Low quality- This study attempted to control for biases but is a cross sectional design.

Conclusion

The studies with the highest quality ratings generally find an association between PTSD and marijuana use but the study designs do not allow for determination if one causes or aggravates the other, or if both are associated with some unknown third factor. We could not find any research that directly addressed the key questions of the benefits and harms of marijuana use for treatment of PTSD. The most relevant literature generally was of low or very low quality and no conclusions can be drawn about the benefits or harms of marijuana use for the treatment of PTSD.

Current Recommended Treatments for PTSD

A search was conducted of the Clinical Guideline Clearinghouse for treatment guidelines for PTSD. Below is a list of the guidelines. See Appendix 4 and Appendix 5.

1. American Psychiatric Association. Practice guideline for the treatment of patients with acute stress disorder and posttraumatic stress disorder. Arlington (VA): American Psychiatric Association; 2004 Nov. 57 p. [463 references]
2. Management of Post-Traumatic Stress Working Group. VA/DoD clinical practice guideline for management of post-traumatic stress. Washington (DC): Veterans Health Administration, Department of Defense; 2010. 251 p.

Appendices

Appendix 1 – Search Strategies

The Cochrane Library Search Description

Includes the following databases: Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, Cochrane Methodology Register, Health Technology Assessment Database, NHS Economic Evaluation Database, and About The Cochrane Collaboration (Cochrane Groups).

Date & Time
May 22nd, 2012 at 12pm-1pm
May 23rd, 2012 at 4pm-5pm

Limits
Adulthood (18 yrs & older)
English
Human

Search
1. "Cannabis"[Mesh]
2. "Cannabis Smoking"[Mesh]
3. (#1) OR (#2) (3624)
4. "Stress disorders, post-traumatic"[Mesh] (8925)
5. (#3) AND (#4) (1,0,1,0,0,0,0)

Total articles identified in The Cochrane Library = 2

1. Hetrick SE, Purcell R, Garner B, Parslow R. Combined pharmacotherapy and psychological therapies for post traumatic stress disorder (PTSD). Cochrane Database of Systematic Reviews 2010, Issue 7. Art. No.: CD007316. DOI: 10.1002/14651858.CD007316.pub2.
2. Schiff M, Zweig HH, Benbenishty R, Hasin DS. Exposure to terrorism and israeli youths' cigarette, alcobol, and cannabis use. Am J Public Health. 2007 Oct;97(10):1852-8.

Ovid MEDLINE® Search Description

Date & Time
May 9th, 2012 at 8am-12pm
May 22nd, 2012 at 2:30pm-5pm

Limits
All Adults (19+)
English
Human

Mesh Terms
Note: **automatic explosion (explode)** - In PubMed, MeSH (Medical Subject Headings) terms (as well as any subheading that is the top of a "subheading tree") are "exploded"

automatically to retrieve citations that carry the specified MeSH heading (or subheading) and also retrieve citations that carry any of the more specific MeSH headings (or subheadings) indented beneath it in the Tree structure.

1. Stress Disorders, Post-Traumatic
2. Cannabis
3. Marijuana Abuse
4. Marijuana Smoking
5. Tetrahydrocannabinol
6. Sativex (Supplementary Concept)

Stress Disorders, Post-Traumatic Entry Terms:

- Post-Traumatic Stress Disorder
- Stress Disorder, Post-Traumatic
- Stress Disorders, Post Traumatic
- PTSD
- Stress Disorder, Post Traumatic
- Neuroses, Posttraumatic
- Posttraumatic Neuroses
- Posttraumatic Stress Disorders
- Posttraumatic Stress Disorder
- Stress Disorder, Posttraumatic
- Stress Disorders, Posttraumatic
- Neuroses, Post-Traumatic
- Neuroses, Post Traumatic
- Post-Traumatic Neuroses
- Post-Traumatic Stress Disorders
- Post Traumatic Stress Disorders
- Chronic Post-Traumatic Stress Disorder
- Chronic Post Traumatic Stress Disorder
- Delayed Onset Post-Traumatic Stress Disorder
- Delayed Onset Post Traumatic Stress Disorder
- Acute Post-Traumatic Stress Disorder
- Acute Post Traumatic Stress Disorder

Cannabis Entry Terms:

- Cannabi
- Hemp Plant
- Hemp Plants
- Plant, Hemp
- Plants, Hemp
- Cannabis indica
- Cannabis indicas
- indica, Cannabis
- indicas, Cannabis
- Marihuana

- Marihuanas
- Marijuana
- Marijuanas
- Ganja
- Ganjas
- Hashish
- Hashishs
- Hemp
- Hemps
- Bhang
- Bhangs
- Cannabis sativa
- Cannabis sativas
- sativa, Cannabis
- sativas, Cannabis

Marijuana Abuse Entry Terms:

- Abuse, Marijuana
- Marihuana Abuse
- Abuse, Marihuana
- Hashish Abuse
- Abuse, Hashish
- Cannabis-Related Disorder
- Cannabis Related Disorder
- Disorder, Cannabis-Related
- Cannabis Abuse
- Abuse, Cannabis
- Cannabis Dependence
- Dependence, Cannabis
- Marijuana Dependence
- Dependence, Marijuana

Marijuana Smoking Entry Terms:

- Smoking, Marijuana
- Marihuana Smoking
- Smoking, Marihuana
- Cannabis Smoking
- Smoking, Cannabis
- Hashish Smoking
- Smoking, Hashish

Tetrahydrocannabinol Entry Terms:

- delta(1)-Tetrahydrocannabinol
- THC
- delta(9)-Tetrahydrocannabinol

- delta(9)-THC
- Dronabinol
- 9-ene-Tetrahydrocannabinol
- 9 ene Tetrahydrocannabinol
- delta(1)-THC
- Tetrahydrocannabinol, (6a-trans)-Isomer
- Tetrahydrocannabinol, Trans-Isomer
- Tetrahydrocannabinol, Trans Isomer
- Tetrahydrocannabinol, (6aS-cis)-Isomer
- Tetrahydrocannabinol, Trans-(+-)-Isomer
- Marinol
- Solvay Brand of Tetrahydrocannabinol
- Tetrahydrocannabinol, (6aR-cis)-Isomer

Supplementary Concept
Tetrahydrocannabinol-cannabidiol combination"[Supplementary Concept]

- Sativex

Search 1

1. "Cannabis/therapeutic use"[Majr] (246)
2. "Stress Disorders, Post-Traumatic/therapy"[Majr] (1,562)
3. (#1) AND (#2) (0)
4. "Cannabis"[Majr] (1,024)
5. (#2) AND (#4) (0)
6. "Stress Disorders, Post-Traumatic"[Majr] (7,756)
7. (#4) AND (#6) (0)
8. "Marijuana Smoking"[Majr] (734)
9. (#6) AND (#8) (3)
10. "Marijuana Abuse"[Majr] (1,292)
11. (#6) AND (#10) (4)
12. "Tetrahydrocannabinol"[Majr] (555)
13. (#6) AND (#12) (0)
14. "tetrahydrocannabinol-cannabidiol combination" [Supplementary Concept] (15)
15. (#6) AND (#14) (0)

Total articles identified in Search 1 = 7
Note: All seven articles were saved into RefWorks. I am now going to broaden my search. Instead of restricting my search to major topics [Mojr] I am going to use [Mesh] terms.

Search 2

1. "Cannabis/therapeutic use"[Mesh] (348)
2. "Stress Disorders, Post-Traumatic/therapy"[Mesh] (2,366)
3. (#1) and (#2) (1)
4. "Cannabis"[Mesh] (1,563)

5. "Stress Disorders, Post-Traumatic"[Mesh] (9,494)
6. (#4) and (#5) (4)
7. "Marijuana Smoking"[Mesh] (979)
8. (#5) AND (#7) (4)
9. "Marijuana Abuse"[Mesh] (1,932)
10. (#5) AND (#9) (11)
11. "Tetrahydrocannabinol"[Mesh] (827)
12. (#5) AND (#11) (0)
13. "tetrahydrocannabinol-cannabidiol combination" [Supplementary Concept] (15)
14. (#5) AND (#13) (0)

Total articles identified in Search 2 = 20
Note: The 20 newly identified articles were added to the previously identified articles in RefWorks (a total of 27 articles).

Search 3

Note: In order to make sure no articles were missed I searched for "Stress Disorders, Post-Traumatic"[Mesh] AND "cannabis" OR "marijuana." This search is a combination of a mesh search and text word searching.

1. "Cannabis" (3,599)
2. "Marijuana" (4,410)
3. (#1) OR (#2) (6,251)
4. "Stress Disorders, Post-Traumatic"[Mesh] (9,496)
5. (#3) AND (#4) (36)

Total articles identified in Search 3 = 36
These 36 articles were added to the ones already in RefWorks.

Search 4

1. "Cannabis" (3,599)
2. "Marijuana" (4,410)
3. (#1) OR (#2) (6,251)
4. "Post-traumatic stress disorder" (2,102)
5. "PTSD" (6,067)
6. (#4) AND (#5) (6,743)
7. (#3) AND (#6) (34)

Total articles identified in Search 4 = 34
These 34 articles were added to RefWorks.

Of the 97 articles identified in Search 1, 2, 3 and 4, 50 were exact duplicates. Below are the 47 unique articles that will be analyzed and included in the evidence review.

1. Apfel BA, Ross J, Hlavin J, Meyerhoff DJ, Metzler TJ, Marmar CR, et al. Hippocampal volume differences in gulf war veterans with current versus lifetime posttraumatic stress disorder symptoms. Biol Psychiatry. 2011 Mar 15;69(6):541-8.
2. Barrett EL, Mills KL, Teesson M. Hurt people who hurt people: Violence amongst individuals with comorbid substance use disorder and post traumatic stress disorder. Addict Behav. 2011 Jul;36(7):721-8.
3. Bonn-Miller MO, Vujanovic AA, Boden MT, Gross JJ. Posttraumatic stress, difficulties in emotion regulation, and coping-oriented marijuana use. Cogn Behav Ther. 2011 Mar;40(1):34-44.
4. Bonn-Miller MO, Vujanovic AA, Feldner MT, Bernstein A, Zvolensky MJ. Posttraumatic stress symptom severity predicts marijuana use coping motives among traumatic event-exposed marijuana users. J Trauma Stress. 2007 Aug;20(4):577-86.
5. Brady K, Casto S, Lydiard RB, Malcolm R, Arana G. Substance abuse in an inpatient psychiatric sample. Am J Drug Alcohol Abuse. 1991;17(4):389-97.
6. Bremner JD, Southwick SM, Darnell A, Charney DS. Chronic PTSD in vietnam combat veterans: Course of illness and substance abuse. Am J Psychiatry. 1996 Mar;153(3):369-75.
7. Calhoun PS, Sampson WS, Bosworth HB, Feldman ME, Kirby AC, Hertzberg MA, et al. Drug use and validity of substance use self-reports in veterans seeking help for posttraumatic stress disorder. J Consult Clin Psychol. 2000 Oct;68(5):923-7.
8. Chen KW, Banducci AN, Guller L, Macatee RJ, Lavelle A, Daughters SB, et al. An examination of psychiatric comorbidities as a function of gender and substance type within an inpatient substance use treatment program. Drug Alcohol Depend. 2011 Nov 1;118(2-3):92-9.
9. Cornelius JR, Kirisci L, Reynolds M, Clark DB, Hayes J, Tarter R. PTSD contributes to teen and young adult cannabis use disorders. Addict Behav. 2010 Feb;35(2):91-4.
10. Corstorphine E, Waller G, Lawson R, Ganis C. Trauma and multi-impulsivity in the eating disorders. Eat Behav. 2007 Jan;8(1):23-30.
11. Cougle JR, Bonn-Miller MO, Vujanovic AA, Zvolensky MJ, Hawkins KA. Posttraumatic stress disorder and cannabis use in a nationally representative sample. Psychol Addict Behav. 2011 Sep;25(3):554-8.
12. Eaton NR, Krueger RF, Keyes KM, Skodol AE, Markon KE, Grant BF, et al. Borderline personality disorder co-morbidity: Relationship to the internalizing-externalizing structure of common mental disorders. Psychol Med. 2011 May;41(5):1041-50.
13. Falck RS, Wang J, Siegal HA, Carlson RG. The prevalence of psychiatric disorder among a community sample of crack cocaine users: An exploratory study with practical implications. J Nerv Ment Dis. 2004 Jul;192(7):503-7.
14. Foster EM. Deployment and the citizen soldier: Need and resilience. Med Care. 2011 Mar;49(3):301-12.
15. Gil-Rivas V, Fiorentine R, Anglin MD. Sexual abuse, physical abuse, and posttraumatic stress disorder among women participating in outpatient drug abuse treatment. J Psychoactive Drugs. 1996 Jan-Mar;28(1):95-102.
16. Greenfield SF, Back SE, Lawson K, Brady KT. Substance abuse in women. Psychiatr Clin North Am. 2010 Jun;33(2):339-55.
17. Johnson SD, Striley C, Cottler LB. The association of substance use disorders with trauma exposure and PTSD among african american drug users. Addict Behav. 2006 Nov;31(11):2063-73.
18. Khoury L, Tang YL, Bradley B, Cubells JF, Ressler KJ. Substance use, childhood traumatic experience, and posttraumatic stress disorder in an urban civilian population. Depress Anxiety. 2010 Dec;27(12):1077-86.
19. Kidorf M, Disney ER, King VL, Neufeld K, Beilenson PL, Brooner RK. Prevalence of psychiatric and substance use disorders in opioid abusers in a community syringe exchange program. Drug Alcohol Depend. 2004 May 10;74(2):115-22.
20. Koenen KC, Lyons MJ, Goldberg J, Simpson J, Williams WM, Toomey R, et al. Co-twin control study of relationships among combat exposure, combat-related PTSD, and other mental disorders. J Trauma Stress. 2003 Oct;16(5):433-8.
21. Lewis CF. Post-traumatic stress disorder in HIV-positive incarcerated women. J Am Acad Psychiatry Law. 2005;33(4):455-64.
22. Lippert AM, Fendrich M, Johnson TP. Vicarious exposure to terrorist attacks and substance use: Results from an urban household survey. J Urban Health. 2008 May;85(3):411-27.
23. Lipschitz DS, Rasmusson AM, Anyan W, Cromwell P, Southwick SM. Clinical and functional correlates of posttraumatic stress disorder in urban adolescent girls at a primary care clinic. J Am Acad Child Adolesc Psychiatry. 2000 Sep;39(9):1104-11.
24. Lipschitz DS, Rasmusson AM, Anyan W, Gueorguieva R, Billingslea EM, Cromwell PF, et al. Posttraumatic stress disorder and substance use in inner-city adolescent girls. J Nerv Ment Dis. 2003 Nov;191(11):714-21.
25. Magliozzi JR, Kanter SL, Csernansky JG, Hollister LE. Detection of marijuana use in psychiatric patients by determination of urinary delta-9-tetrahydrocannabinol-11-oic acid. J Nerv Ment Dis. 1983 Apr;171(4):246-9.
26. Marshall RD, Galea S. Science for the community: Assessing mental health after 9/11. J Clin Psychiatry. 2004;65 Suppl 1:37-43.

27. Meghani SH, Wiedemer NL, Becker WC, Gracely EJ, Gallagher RM. Predictors of resolution of aberrant drug behavior in chronic pain patients treated in a structured opioid risk management program. Pain Med. 2009 Jul-Aug;10(5):858-65.

28. Moffitt TE, Caspi A, Taylor A, Kokaua J, Milne BJ, Polanczyk G, et al. How common are common mental disorders? evidence that lifetime prevalence rates are doubled by prospective versus retrospective ascertainment. Psychol Med. 2010 Jun;40(6):899-909.

29. Najavits LM, Harned MS, Gallop RJ, Butler SF, Barber JP, Thase ME, et al. Six-month treatment outcomes of cocaine-dependent patients with and without PTSD in a multisite national trial. J Stud Alcohol Drugs. 2007 May;68(3):353-61.

30. Norman SB, Tate SR, Anderson KG, Brown SA. Do trauma history and PTSD symptoms influence addiction relapse context? Drug Alcohol Depend. 2007 Sep 6;90(1):89-96.

31. Okulate GT, Jones DB. Post-traumatic stress disorder, survivor guilt and substance use--a study of hospitalised nigerian army veterans. S Afr Med J. 2006 Feb;96(2):144-6.

32. Peters RJ,Jr, Meshack A, Amos C, Scott-Gurnell K, Savage C, Ford K. The association of drug use and post-traumatic stress reactions due to hurricane ike among fifth ward houstonian youth. J Ethn Subst Abuse. 2010;9(2):143-51.

33. Pierre JM. Psychosis associated with medical marijuana: Risk vs. benefits of medicinal cannabis use. Am J Psychiatry. 2010 May;167(5):598-9.

34. Potter CM, Vujanovic AA, Marshall-Berenz EC, Bernstein A, Bonn-Miller MO. Posttraumatic stress and marijuana use coping motives: The mediating role of distress tolerance. J Anxiety Disord. 2011 Apr;25(3):437-43.

35. Resnick HS, Acierno R, Amstadter AB, Self-Brown S, Kilpatrick DG. An acute post-sexual assault intervention to prevent drug abuse: Updated findings. Addict Behav. 2007 Oct;32(10):2032-45.

36. Rhoades H, Wenzel SL, Golinelli D, Tucker JS, Kennedy DP, Green HD, et al. The social context of homeless men's substance use. Drug Alcohol Depend. 2011 Nov 1;118(2-3):320-5.

37. Rigby E, Reid L, Schipperheijn JA, Weston L, Ikkos G. Clinical librarians: A journey through a clinical question. Health Info Libr J. 2002 Sep;19(3):158-60.

38. Sartor CE, McCutcheon VV, Pommer NE, Nelson EC, Duncan AE, Waldron M, et al. Posttraumatic stress disorder and alcohol dependence in young women. J Stud Alcohol Drugs. 2010 Nov;71(6):810-8.

39. Shand FL, Degenhardt L, Slade T, Nelson EC. Sex differences amongst dependent heroin users: Histories, clinical characteristics and predictors of other substance dependence. Addict Behav. 2011 Jan-Feb;36(1-2):27-36.

40. Tepe E, Dalrymple K, Zimmerman M. The impact of comorbid cannabis use disorders on the clinical presentation of social anxiety disorder. J Psychiatr Res. 2012 Jan;46(1):50-6.

41. Trafton JA, Minkel J, Humphreys K. Opioid substitution treatment reduces substance use equivalently in patients with and without posttraumatic stress disorder. J Stud Alcohol. 2006 Mar;67(2):228-35.

42. Vetter S, Rossegger A, Rossler W, Bisson JI, Endrass J. Exposure to the tsunami disaster, PTSD symptoms and increased substance use - an internet based survey of male and female residents of switzerland. BMC Public Health. 2008 Mar 19;8:92.

43. Villagonzalo KA, Dodd S, Ng F, Mihaly S, Langbein A, Berk M. The relationship between substance use and posttraumatic stress disorder in a methadone maintenance treatment program. Compr Psychiatry. 2011 Sep-Oct;52(5):562-6.

44. Vlahov D, Galea S, Ahern J, Resnick H, Boscarino JA, Gold J, et al. Consumption of cigarettes, alcohol, and marijuana among new york city residents six months after the september 11 terrorist attacks. Am J Drug Alcohol Abuse. 2004 May;30(2):385-407.

45. Vlahov D, Galea S, Resnick H, Ahern J, Boscarino JA, Bucuvalas M, et al. Increased use of cigarettes, alcohol, and marijuana among manhattan, new york, residents after the september 11th terrorist attacks. Am J Epidemiol. 2002 Jun 1;155(11):988-96.

46. Xian H, Scherrer JF, Grant JD, Eisen SA, True WR, Jacob T, et al. Genetic and environmental contributions to nicotine, alcohol and cannabis dependence in male twins. Addiction. 2008 Aug;103(8):1391-8.

47. Yap MB, Reavley NJ, Jorm AF. Young people's beliefs about the harmfulness of alcohol, cannabis and tobacco for mental disorders: Findings from two australian national youth surveys. Addiction. 2012 Apr;107(4):838-47.

PsycINFO/EBESCO Host Search Description

Date & Time

May 22nd, 2012 at 11am-12pm

Limits

Adulthood (18 yrs & older)

English

Human

Search

1. MJ "cannabis" (923)
2. MJ "marijuana" (2767)
3. S1 OR S2 (3624)
4. MJ "posttraumatic stress disorder" (8925)
5. (S1 or S2) AND (S3 and S4) (7)

Total articles identified in PsychINFO = 7

1. Bonn-Miller MO, Vujanovic AA, Boden MT, Gross JJ. Posttraumatic stress, difficulties in emotion regulation, and coping-oriented marijuana use. Cogn Behav Ther. 2011 Mar;40(1):34-44.
2. Bonn-Miller MO, Vujanovic AA, Drescher, Kent D. Cannabis use among military veterans after residential treatment for posttraumatic stress disorder. Psychol Addict Behav. 2011 September;23(3):485-91.
3. Bonn-Miller MO, Vujanovic AA, Feldner MT, Bernstein A, Zvolensky MJ. Posttraumatic stress symptom severity predicts marijuana use coping motives among traumatic event-exposed marijuana users. J Trauma Stress. 2007 Aug;20(4):577-86.
4. Cornelius JR, Kirisci L, Reynolds M, Clark DB, Hayes J, Tarter R. PTSD contributes to teen and young adult cannabis use disorders. Addict Behav. 2010 Feb;35(2):91-4.
5. Cougle JR, Bonn-Miller MO, Vujanovic AA, Zvolensky MJ, Hawkins KA. Posttraumatic stress disorder and cannabis use in a nationally representative sample. Psychol Addict Behav. 2011 Sep;25(3):554-8.
6. Potter CM, Vujanovic AA, Marshall-Berenz EC, Bernstein A, Bonn-Miller MO. Posttraumatic stress and marijuana use coping motives: The mediating role of distress tolerance. J Anxiety Disord. 2011 Apr;25(3):437-43.
7. Vujanovic AA, Bonn-Miller MO, Marlatt GA. Posttraumatic stress and alcohol use coping motives among a trauma-exposed community sample: The mediating role of non-judgmental acceptance. Addict Behav. 2011 Jul;36(7):707-12.

Articles #2 and #7 were the only articles not previously identified by the PubMed search. The two articles added to the list of articles to be reviewed.

Gray Literature Search

Google Scholar for articles with all of the words "post traumatic stress disorder" AND cannabis = About 8,740 results (0.13 sec). The strategy for the gray literature search was to skim the titles of the articles. If an article seemed to address the benefit or harm of cannabis use among the PTSD population then it would be read and examined. We found only articles that had already been identified through the previous searches.

Appendix 2 – GRADE Methodology

Study Design	Quality of Evidence	Lower if	Higher if
Randomized trial →	High	Risk of bias -1 Serious -2 Very serious Inconsistency -1 Serious -2 Very serious Indirectness -1 Serious -2 Very serious Imprecision -1 Serious -2 Very serious Publication bias -1 Likely -2 Very likely	Large effect +1 Large +2 Very Large Dose response +1 Evidence of a gradient All plausible confounding +1 Would reduce a demonstrated effect or +1 Would suggest a spurious effect when results show no effect
	Moderate		
Observational study →	Low		
	Very Low		

Reference: Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol. 2011 Apr;64(4):383-94.

Appendix 3 – Exclusion reasoning

The studies below are numbered using the search findings in Appendix 2.

Database	Study	Exclusion reasoning
The Cochrane Library	1. Hetrick SE, Purcell R, Garner B, Parslow R. Combined pharmacotherapy and psychological therapies for post traumatic stress disorder (PTSD). Cochrane Database of Systematic Reviews 2010, Issue 7. Art. No.: CD007316. DOI: 10.1002/14651858.CD007316.pub2.	This study did not address the key questions.
The Cochrane Library	2. Schiff M, Zweig HH, Benbenishty R, Hasin DS. Exposure to terrorism and israeli youths' cigarette, alcohol, and cannabis use. Am J Public Health. 2007 Oct;97(10):1852-B.	Excluded because the study was about youth not adults.
PubMed	1. Apfel BA, Ross J, Hlavin J, Meyerhoff DJ, Metzler TJ, Marmar CR, et al. Hippocampal volume differences in gulf war veterans with current versus lifetime posttraumatic stress disorder symptoms. Biol Psychiatry. 2011 Mar 15;69(6):541-8.	This study did not address the key questions.
PubMed	2. Barrett EL, Mills KL, Teesson M. Hurt people who hurt people: Violence amongst individuals with comorbid substance use disorder and post traumatic stress disorder. Addict Behav. 2011 Jul;36(7):721-8.	This study did not address the key questions.
PubMed	5. Brady K, Casto S, Lydiard RB, Malcolm R, Arana G. Substance abuse in an inpatient psychiatric sample. Am J Drug Alcohol Abuse. 1991;17(4):3B9-97.	This study did not address the key questions.
PubMed	7. Calhoun PS, Sampson WS, Bosworth HB, Feldman ME, Kirby AC, Hertzberg MA, et al. Drug use and validity of substance use self-reports in veterans seeking help for posttraumatic stress disorder. J Consult Clin Psychol. 2000 Oct;6B(5):923-7.	This study did not address the key questions.
PubMed	B. Chen KW, Banducci AN, Guller L, Macatee RJ, Lavelle A, Daughters SB, et al. An examination of psychiatric comorbidities as a function of gender and substance type within an inpatient substance use treatment program. Drug Alcohol Depend. 2011 Nov 1;11B(2-3):92-9.	This study did not address the key questions.
PubMed	10. Corstorphine E, Waller G, Lawson R, Ganis C. Trauma and multi-impulsivity in the eating disorders. Eat Behav. 2007 Jan;B(1):23-30.	This study did not address the key questions.
PubMed	12. Eaton NR, Krueger RF, Keyes KM, Skodol AE, Markon KE, Grant BF, et al. Borderline personality disorder co-morbidity: Relationship to the internalizing-externalizing structure of common mental disorders. Psychol Med. 2011 May;41(5):1041-50.	This study did not address the key questions.

PubMed	13. Falck RS, Wang J, Siegal HA, Carlson RG. The prevalence of psychiatric disorder among a community sample of crack cocaine users: An exploratory study with practical implications. J Nerv Ment Dis. 2004 Jul;192(7):503-7.	Excluded because study addressed crack cocaine use and not marijuana use.
PubMed	14. Foster EM. Deployment and the citizen soldier: Need and resilience. Med Care. 2011 Mar;49(3):301-12.	This study did not address the key questions.
PubMed	15. Gil-Rivas V, Fiorentine R, Anglin MD. Sexual abuse, physical abuse, and posttraumatic stress disorder among women participating in outpatient drug abuse treatment. J Psychoactive Drugs. 1996 Jan-Mar;28(1):95-102.	This study did not address the key questions.
PubMed	16. Greenfield SF, Back SE, Lawson K, Brady KT. Substance abuse in women. Psychiatr Clin North Am. 2010 Jun;33(2):339-55.	This study did not address the key questions.
PubMed	18. Khoury L, Tang YL, Bradley B, Cubells JF, Ressler KJ. Substance use, childhood traumatic experience, and posttraumatic stress disorder in an urban civilian population. Depress Anxiety. 2010 Dec;27(12):1077-86.	This study did not address the key questions.
PubMed	19. Kidorf M, Disney ER, King VL, Neufeld K, Beilenson PL, Brooner RK. Prevalence of psychiatric and substance use disorders in opioid abusers in a community syringe exchange program. Drug Alcohol Depend. 2004 May 10;74(2):115-22.	This study did not address the key questions.
PubMed	20. Koenen KC, Lyons MJ, Goldberg J, Simpson J, Williams WM, Toomey R, et al. Co-twin control study of relationships among combat exposure, combat-related PTSD, and other mental disorders. J Trauma Stress. 2003 Oct;16(5):433-8.	This study did not address the key questions.
PubMed	21. Lewis CF. Post-traumatic stress disorder in HIV-positive incarcerated women. J Am Acad Psychiatry Law. 2005;33(4):455-64.	This study did not address the key questions.
PubMed	22. Lippert AM, Fendrich M, Johnson TP. Vicarious exposure to terrorist attacks and substance use: Results from an urban household survey. J Urban Health. 2008 May;85(3):411-27.	This study did not address the key questions.
PubMed	23. Lipschitz DS, Rasmusson AM, Anyan W, Cromwell P, Southwick SM. Clinical and functional correlates of posttraumatic stress disorder in urban adolescent girls at a primary care clinic. J Am Acad Child Adolesc Psychiatry. 2000 Sep;39(9):1104-11.	This study did not address the key questions.
PubMed	24. Lipschitz DS, Rasmusson AM, Anyan W, Gueorguieva R, Billingslea EM, Cromwell PF, et al. Posttraumatic stress disorder and substance use in inner-city adolescent girls. J Nerv Ment Dis. 2003 Nov;191(11):714-21.	This study did not address the key questions.
PubMed	25. Magliozzi JR, Kanter SL, Csernansky JG, Hollister LE. Detection of marijuana use in psychiatric patients by determination of urinary delta-9-tetrahydrocannabinol-11-oic acid. J Nerv Ment Dis. 1983 Apr;171(4):246-9.	This study did not address the key questions.

PubMed	26. Marshall RD, Galea S. Science for the community: Assessing mental health after 9/11. J Clin Psychiatry. 2004;6S Suppl 1:37-43.	This study did not address the key questions.
PubMed	27. Meghani SH, Wiedemer NL, Becker WC, Gracely EJ, Gallagher RM. Predictors of resolution of aberrant drug behavior in chronic pain patients treated in a structured opioid risk management program. Pain Med. 2009 Jul-Aug;10(S):858-6S.	This study did not address the key questions.
PubMed	28. Moffitt TE, Caspi A, Taylor A, Kokaua J, Milne BJ, Polanczyk G, et al. How common are common mental disorders? evidence that lifetime prevalence rates are doubled by prospective versus retrospective ascertainment. Psychol Med. 2010 Jun;40(6):899-909.	This study did not address the key questions.
PubMed	29. Najavits LM, Harned MS, Gallop RJ, Butler SF, Barber JP, Thase ME, et al. Six-month treatment outcomes of cocaine-dependent patients with and without PTSD in a multisite national trial. J Stud Alcohol Drugs. 2007 May;68(3):3S3-61.	This study did not address the key questions.
PubMed	30. Norman SB, Tate SR, Anderson KG, Brown SA. Do trauma history and PTSD symptoms influence addiction relapse context? Drug Alcohol Depend. 2007 Sep 6;90(1):89-96.	This study did not address the key questions.
PubMed	31. Okulate GT, Jones DB. Post-traumatic stress disorder, survivor guilt and substance use--a study of hospitalised nigerian army veterans. S Afr Med J. 2006 Feb;96(2):144-6.	This study did not address the key questions.
PubMed	32. Peters RJ,Jr, Meshack A, Amos C, Scott-Gurnell K, Savage C, Ford K. The association of drug use and post-traumatic stress reactions due to hurricane ike among fifth ward houstonian youth. J Ethn Subst Abuse. 2010;9(2):143-51.	This study did not address the key questions.
PubMed	33. Pierre JM. Psychosis associated with medical marijuana: Risk vs. benefits of medicinal cannabis use. Am J Psychiatry. 2010 May;167(S):S98-9.	This study did not address the key questions.
PubMed	3S. Resnick HS, Acierno R, Amstadter AB, Self-Brown S, Kilpatrick DG. An acute post-sexual assault intervention to prevent drug abuse: Updated findings. Addict Behav. 2007 Dct;32(10):2032-4S.	This study did not address the key questions.
PubMed	36. Rhoades H, Wenzel SL, Golinelli D, Tucker JS, Kennedy DP, Green HD, et al. The social context of homeless men's substance use. Drug Alcohol Depend. 2011 Nov 1;118(2-3):320-S.	This study did not address the key questions.
PubMed	37. Rigby E, Reid L, Schipperheijn JA, Weston L, Ikkos G. Clinical librarians: A journey through a clinical question. Health Info Libr J. 2002 Sep;19(3):158-60.	This study did not address the key questions.
PubMed	38. Sartor CE, McCutcheon VV, Pommer NE, Nelson EC, Duncan AE, Waldron M, et al. Posttraumatic stress disorder and alcohol dependence in young women. J Stud Alcohol Drugs. 2010 Nov;71(6):810-8.	Excluded because study addressed alcohol use and not marijuana use.
PubMed	39. Shand FL, Degenhardt L, Slade T, Nelson EC. Sex differences amongst dependent heroin users: Histories, clinical characteristics and predictors of other substance dependence. Addict Behav. 2011 Jan-Feb;36(1-2):27-36.	This study did not address the key questions.

PubMed	40. Tepe E, Dalrymple K, Zimmerman M. The impact of comorbid cannabis use disorders on the clinical presentation of social anxiety disorder. J Psychiatr Res. 2012 Jan;46(1):50-6.	This study did not address the key questions.
PubMed	41. Trafton JA, Minkel J, Humphreys K. Opioid substitution treatment reduces substance use equivalently in patients with and without posttraumatic stress disorder. J Stud Alcohol. 2006 Mar;67(2):228-35.	This study did not address the key questions.
PubMed	42. Vetter S, Rossegger A, Rossler W, Bisson JI, Endrass J. Exposure to the tsunami disaster, PTSD symptoms and increased substance use - an internet based survey of male and female residents of switzerland. BMC Public Health. 2008 Mar 19;8:92.	This study did not address the key questions.
PubMed	47. Yap MB, Reavley NJ, Jorm AF. Young people's beliefs about the harmfulness of alcohol, cannabis and tobacco for mental disorders: Findings from two australian national youth surveys. Addiction. 2012 Apr;107(4):838-47.	This study did not address the key questions.
PsycINFO	7. Vujanovic AA, Bonn-Miller MO, Marlatt GA. Posttraumatic stress and alcohol use coping motives among a trauma-exposed community sample: The mediating role of non-judgmental acceptance. Addict Behav. 2011 Jul;36(7):707-12.	Excluded because study addressed alcohol use and not marijuana use.

Appendix 4 – APA Specific Treatment Strategies

SPECIFIC TREATMENT STRATEGIES

Reference: American Psychiatric Association. Practice guideline for the treatment of patients with acute stress disorder and posttraumatic stress disorder. Arlington (VA): American Psychiatric Association; 2004 Nov. 57 p. [463 references]

1. Psychopharmacology

a) SSRIs. Evidence from several large randomized, double- blind controlled trials suggests that SSRIs are first-line medication treatment for both men and women with PTSD (123, 141–147). There are four reasons that SSRIs are the current medications of choice for PTSD: 1) they ameliorate all three PTSD symptom clusters (i.e., re-experiencing, avoidance/numbing, and hyperarousal), 2) they are effective treatments for psychiatric disorders that are frequently comorbid with PTSD (e.g., depression, panic disorder, social phobia, and obsessive-compulsive disorder), 3) they may reduce clinical symptoms (such as suicidal, impulsive, and aggressive behaviors) that often complicate management of PTSD, and 4) they have relatively few side effects.

Reductions in the severity of core PTSD symptoms have been shown with fluoxetine, sertraline, and paroxetine in studies that were of relatively short duration (8–12 weeks) and included predominantly women with chronic PTSD resulting from rape or assault (123, 141–146, 148). While symptom reduction was generally observed within 2–4 weeks of treatment, symptoms of anger and irritability were reduced within the first week (149). In studies of fluoxetine, improvement in arousal, numbing, and avoidance (but not re-experiencing) and overall response were greater in women than in men. Other studies have demonstrated efficacy for these agents in intrusive, avoidance/ numbing, and arousal symptoms. Smaller open-label studies of fluvoxamine have shown efficacy in sleep-related symptoms (including nightmares) in combat veterans (147, 150). Head-to-head comparisons between any of the SSRIs for ASD or PTSD symptoms have not been published; however, clinical consensus holds that these agents differ primarily in their pharmacokinetics, metabolic effects on other medications, and side effects rather than in their efficacy in treating ASD or PTSD.

b) Tricyclic antidepressants and MAOIs. Studies of tri- cyclic antidepressants demonstrated efficacy for amitriptyline and imipramine (151, 152) but not desipramine (153). With the MAOIs, limited data suggest the efficacy of phenelzine and brofaromine (an MAOI available in Europe) (154, 155). In all of the trials, subjects were primarily male combat veterans, which limits the generalizability of findings. There do not appear to be studies of the effects of either MAOIs or tricyclic antidepressants specifically in women with PTSD or ASD.

c) Benzodiazepines. While benzodiazepines can reduce anxiety and improve sleep, their efficacy in preventing PTSD or treating the core symptoms of PTSD has been neither established nor adequately evaluated (156, 157). Concerns about addictive potential in individuals with comorbid substance use disorders may prompt additional caution regarding the use of benzodiazepines. Worsening of symptoms with benzodiazepine discontinuation has also been reported (158). However, in a naturalistic study of more than 300 veterans with PTSD and comorbid sub- stance abuse, treatment with benzodiazepines was not associated with adverse effects on outcome (159).

d) Anticonvulsants. Dpen-label studies of divalproex, carbamazepine, and topiramate have demonstrated mixed or limited efficacy with regard to specific symptom clusters of PTSD (160–162), but these studies, as well as a single controlled trial of lamotrigine (163), have indicated benefit with regard to the re-experiencing symptoms.

e) Antipsychotics. Psychotic symptoms are not included in the diagnostic criteria for either ASD or PTSD. Nonetheless, patients with these illnesses may also experience psychotic symptoms as part of a comorbid disorder. Before initiating antipsychotic treatment, careful diagnostic evaluation is required to appropriately address the potential contributions of delirium, dementia, primary thought dis- orders, brief psychotic reactions, delusional disorder, sub- stance abuse, closed head injury, or other comorbid general medical conditions. Preliminary studies of the second- generation antipsychotic agents olanzapine (164–166), quetiapine (167), and risperidone (168) in patients with PTSD suggest a potential role for these medications in pharmacological treatment, particularly when concomitant psychotic symptoms are present or when first-line approaches have been ineffective in controlling symptoms.

f) Adrenergic inhibitors. The □□□adrenergic agonists decrease central adrenergic activity and have been proposed for the treatment of PTSD. Preliminary evidence from small open-label studies has shown possible benefits with prazosin (169) and with clonidine in combination with imipramine (170). However, there have been no published controlled studies of these agents to date.

While □□adrenergic blockers are at times prescribed for PTSD (171) and have been used in the treatment of performance anxiety, there have been no controlled studies of these agents for PTSD. Preliminary results suggest that acute administration of propranolol after trauma may reduce some later symptoms of PTSD (137, 172). Further controlled studies are necessary to evaluate this practice before it can be considered a part of the therapeutic armamentarium.

2. Psychotherapeutic interventions

a) Cognitive and behavior therapies. Cognitive behavior therapy in ASD or PTSD targets the distorted threat appraisal process (in some instances through repeated exposure and in others through techniques focusing on in- formation processing without repeated exposure) in an effort to desensitize the patient to trauma-related triggers.

Distinctions may be drawn between psychotherapies that focus principally on aspects of cognitive processing and those that emphasize behavioral techniques. However, aspects of both are frequently combined, and studies that identify the effective components of these therapies or that distinguish one from another are not available. A course of cognitive behavior therapy generally begins with education about the symptoms of the disorder, as well as a rationale for asking the patient to recall painful experiences and relaxation training. After the therapist assesses the patient's ability to tolerate within-session anxiety and temporary exacerbations of symptoms, the patient is led through a series of sessions in which the traumatic event and its aftermath are imagined and described, and the patient is asked to focus on the negative affect and arousal until they subside. Reassurance and relaxation exercises aid the patient in progressing through these sessions, and homework assignments allow the patient to practice out- side the sessions or while confronting triggers of anxiety (specific places or activities) in vivo (125, 173, 174). A limited number of well-designed studies demonstrate some success not only in speeding recovery but also in preventing PTSD when cognitive behavior therapy is given over a few sessions beginning 2–3 weeks after trauma exposure (135, 173, 175–178). Both stress inoculation and prolonged exposure techniques have demonstrated efficacy in women with PTSD resulting from assault or rape (179–181). Prolonged exposure (through imaginal and in vivo expo- sure to avoided situations associated with previous trauma) has been shown to be effective, particularly in the PTSD-associated symptoms of anxiety and avoidance (179, 182). However, several studies have noted that expo- sure may increase rather than decrease symptoms in some individuals (178, 183). Stress inoculation training involving breathing exercises, relaxation training, thought stopping, role playing, and cognitive restructuring has also proven effective alone and in combination with prolonged exposure in reducing PTSD symptoms (179). Survivors of rape, crime victims, and combat veterans have demonstrated improvement in overall PTSD symptoms and nightmares in response to imagery rehearsal (i.e., imaginal prolonged expo- sure) (184, 185). Clinical improvement (but not recovery) was also demonstrated in a group of PTSD patients with di- verse trauma exposures who received either imaginal exposure or cognitive behavior therapy (186, 187). In group settings, cognitive processing therapy designed to correct distortions related to threat appraisal and safety through a facilitated study of the patient's written narrative of his or her traumatic experience has shown promise (188). Most of these trials have been short-term, and the extent to which improvement is maintained over time has not been assessed through follow-up study.

b) Eye movement desensitization and reprocessing (EMDR). EMDR is a form of psychotherapy that includes an exposure-based therapy (with multiple brief, interrupted exposures to traumatic material), eye movement, and recall and verbalization of traumatic memories of an event or events. It therefore combines multiple theoretical perspectives and techniques, including cognitive behavior therapy. Some point to the use of directed eye movements as a feature markedly distinguishing this form of therapy from other cognitive behavior approaches. Others point to the fact that traumatic material need not be verbalized; instead, patients are directed to think about their traumatic experiences without having to discuss them. Like many of the studies of other cognitive behavior and exposure therapies, most of the well-designed EMDR studies have been small, but several meta-analyses have demonstrated efficacy similar to that of other forms of cognitive and behavior therapy (189–192). Studies also suggest that the eye movements are neither necessary nor sufficient to the out- come (193–195), but these findings remain controversial (196, 197). Although it appears that efficacy may be related to the components of the technique common to other exposure based cognitive therapies, as in the previously de- scribed cognitive behavior therapies, further study is necessary to clearly identify the effective subcomponents of combined techniques. Follow-up studies are also needed to determine whether observed improvements are maintained over time.

c) Psychodynamic psychotherapy. Psychodynamic therapy has, from its beginnings, been concerned with responses to traumatic events (198–200). There is an extensive body of research that includes descriptive designs, process-to-outcome correlational studies, and case studies. However, randomized, controlled research on psycho- dynamic psychotherapy in patients with ASD or PTSD is extremely limited. One controlled trial of psychodynamic therapy versus hypnotherapy or desensitization versus no therapy showed all interventions were superior to the control condition (no treatment) in decreasing avoidance and intrusive symptoms (201). Other controlled trials of hypnotherapy for ASD or PTSD have not been published, but descriptive studies and clinical consensus support its use—by appropriately trained individuals—in reducing symptoms of anxiety associated with acute distress and traumatic event cues and as a nonpharmacological adjunctive approach to anxiety reduction (202). A meta-analysis of controlled psychotherapy trials (including the study by Brom et al. [201]) also suggested the efficacy of hypnosis—particularly at the end of therapy (203).

The clinical research and narrative-based literatures on psychodynamic psychotherapy outline two major approaches to the treatment of traumatic stress disorders. The first views an individual's defenses and coping skills as a product of his or her biopsychosocial development and focuses on the meaning of the trauma for the individual in terms of prior psychological conflicts and developmental experience and relationships, as well as the particular developmental time of the traumatic occurrence(s). This approach examines the person's overall capacity to cope with memories of traumatic event(s) and their triggers and the coping style he or she uses to manage these memories (204, 205). The second approach focuses on the effect of traumatic experience on the individual's prior self-object experiences, overwhelmed self-esteem, altered experience of safety, and loss of self-cohesiveness and self-observing functions and helps the person identify and maintain a functional sense of self in the face of trauma (206, 207). Both approaches appear to be useful in addressing the subjective and interpersonal sustaining factors of the ill- ness (e.g., shattered assumptions about attachments, is- sues of trust), as well as the changes in beliefs and world view and the widely altered threat perceptions often seen in chronic PTSD (21, 208, 209). Psychodynamic

psycho- therapists employ a mixture of supportive and insight-oriented interventions based on an assessment of the individual patient's symptoms, developmental history, personality, and available social supports as well as an ongoing assessment of the patient's ability to tolerate exploration of the trauma (210, 211). In chronic PTSD, issues of transference are often explored to help the patient understand conscious and unconscious concerns surrounding the meaning of re- cent and more remote traumatic events in his or her life as they appear in the treatment (212). Awareness of counter- transference is a central component of treatment of traumatic experience in psychodynamic psychotherapy and in other therapies. The therapist's emotional response on hearing the patient describe the traumatic events can either facilitate or disrupt the therapeutic alliance, making ongoing attention to countertransference of particular importance in treating patients with ASD and PTSD.

d) Psychological debriefing. Psychological debriefing was developed as an intervention aimed at preventing the development of the negative emotional sequelae of traumatic events, including ASD and PTSD. This staged, semi- structured group (or, as often administered, individual) interview and educational process includes education about trauma experiences in general and about the chronological facts of the recently experienced traumatic event and exploration of the emotions associated with the event. Since debriefing has received considerable publicity, it may be expected (or specifically requested) by leaders or managers when a group confronts disaster. In the military, for example, group debriefings have been used as a means for describing normative responses to trauma exposures and educating individuals about pursuing further assistance if symptoms persist or cause significant dysfunction or distress. However, well-controlled studies of debriefing that have used single-session, individual, and group de- briefing have not demonstrated efficacy (128, 129, 213– 216). Although some trauma survivors have reported that they experienced such debriefings as helpful, there is no evidence at present that establishes psychological debrief- ing as effective in preventing PTSD or improving social and occupational functioning. In some settings, it has been shown to increase symptoms (217–219). Its use may be most problematic with groups of unknown individuals who have widely varying trauma exposures or when it is administered early after trauma exposure, before safety and decreased arousal are established. Immediately after exposure, persons may not be able to listen attentively, absorb new information, or appreciate the nuances of the demands ahead in a manner that promotes recovery (220, 221). Also, in heterogeneous groups, some individuals will be increasing their exposure through group participation and obtain no added support after the group session, thereby potentially increasing their likelihood of later distress (19).

3. Psychoeducation and support

Supportive interventions are often used as the control intervention in studies of more specific treatments. How- ever, clinical experience indicates that both support and psychoeducation appear to be helpful as early interventions to reduce the psychological sequelae of exposure to mass violence or disaster. When access to expert care is limited by environmental conditions or reduced availability of medical resources, rapid dissemination of educational materials may help many persons to deal effectively with subsyndromal manifestations of trauma exposure. Such educational materials often focus on 1) the expected physiological and emotional response to traumatic events, 2) strategies for decreasing secondary or continuous expo- sure to the traumatic event, 3) stress-reduction techniques such as breathing exercises and physical exercise, 4) the importance of remaining mentally active, 5) the need to concentrate on self-care tasks in the aftermath of trauma, and 6) recommendations for early referral if symptoms persist. Encouraging persons who are acutely traumatized to first rely on their inherent strengths, their existing support net- works, and their own judgment may reduce the need for further intervention. Although the efficacy of these measures alone in prevention of ASD or PTSD is unproven, emphasis on self-reliance and self-care should augment other strategies when and if they become necessary.

Appendix 5 – VA/DoD Clinical Practice Guideline for Management of PTSD

Reference: Management of Post-Traumatic Stress Working Group. VA/DoD clinical practice guideline for management of post-traumatic stress. Washington (DC): Veterans Health Administration, Department of Defense; 2010. 251 p.

Major Recommendations

Note from the Department of Veterans Affairs and the Department of Defense (VA/DoD) and the National Guideline Clearinghouse (NGC): The recommendations for the management of post-traumatic stress are organized into 4 modules with 3 algorithms. The modules with accompanying recommendations are provided below. See the original guideline document for the algorithms and evidence tables associated with selected recommendations, including level and quality of evidence, strength of recommendation, and supporting evidence citations.

The strength of recommendation grading (A, B, C, D, I) is defined at the end of the "Major Recommendations" field.

Core Module: Post-traumatic Stress, Screening

1. **Primary Prevention**
   - A. **Education and Training to Foster Resilience**

     Objective

     Prepare individuals and groups for exposure to potentially traumatic experiences in ways that minimize the likelihood of development of post-traumatic stress disorder (PTSD) and other trauma-related problems.

     Recommendations

     1. In high-risk occupations, for which the probability of trauma exposure is moderate or high, efforts should be undertaken to increase the psychological resilience of workers to the negative effects of trauma exposure.
2. **Populations At-Risk for Developing PTSD**
   - B. **Person Exposed to Trauma**

     Objective

     Assess the nature of the traumatic event and other potential stressors.

     Recommendations

     1. Persons exposed to trauma should be assessed for the type, frequency, nature, and severity of the trauma. **[B]**
        a. Assessment should include a broad range of potential trauma exposures in addition to the index trauma.
        b. Trauma Exposure Assessment instruments may assist in evaluating the nature and severity of the exposure.
        c. Assessment of existing social supports and ongoing stressors is important.
3. **Secondary Prevention**
   - C. **Screen for PTSD Symptoms**

     Objective

     Identify possible cases of post-traumatic stress.

     Recommendations

     1. All new patients should be screened for symptoms of PTSD initially and then on an annual basis or more frequently if clinically indicated due to clinical suspicion, recent trauma exposure (e.g., major disaster), or history of PTSD. **[B]**
     2. Patients should be screened for symptoms of PTSD using paper-and-pencil or computer-based screening tools. **[B]**
     3. There is insufficient evidence to recommend one PTSD screening tool versus another. However, the following screening tools have been validated and should be considered for use. For example (see Appendix C in the original guideline document):
        - Primary Care PTSD Screen (PC-PTSD)
        - PTSD Brief Screen
        - Short Screening Scale for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM IV) PTSD
        - PTSD Checklist (PCL)
     4. There is insufficient evidence to recommend special screening for members of any cultural or racial group or gender. **[I]**
   - D. **Are Trauma-Related Symptoms Present?**

     Objective

     Identify people exposed to trauma who are at risk for developing acute stress reactions (ASR), acute stress disorder (ASD), or PTSD.

     Recommendations

     0. Individuals who are presumed to have symptoms of PTSD or who are positive for PTSD on the initial screening should receive a more detailed assessment of their symptoms.
     1. Useful symptom-related information may include details, such as time of onset, frequency, course, severity, level of distress, and degree of functional impairment.
     2. The elapsed time since the exposure to trauma should be considered when assessing the risk of developing PTSD and determining the diagnosis and appropriate intervention.

     See the original guideline document for definitions that will help providers select the appropriate treatment algorithm.
   - E. **Educate About Additional Care If Needed; Provide Contact Information**

     Objective

     Provide normalization for survivors and responders whose reactions are not clinically significant.

     Recommendations

     0. Pre- and post-trauma education should include helping the asymptomatic trauma survivor or responder understand that the acute stress reactions of other people are common and probably transient and do not indicate personal failure or weakness, mental illness, or health problems.
     1. Education should include sufficient review of the many ways that post-traumatic problems can present, including symptoms in the ASD/PTSD spectrum, behavioral problems with family and friends, occupational problems, and the potential impact of alcohol or other substance misuse/abuse.

2. Education should also include positive messages by identifying and encouraging positive ways of coping, describing simple strategies to resolve or cope with developing symptoms and problems, and setting expectations for mastery and/or recovery.
3. Provide contact information, should post-traumatic symptoms emerge later.
4. Routine debriefing or formal psychotherapy is not beneficial for asymptomatic individuals and may be harmful. **[D]**

Module A: Management of ASR and Prevention of PTSD

1. **Assessment and Triage**

A. **Trauma Exposure (within the past 30 days)**

Acute Stress Reaction (ASR) is a transient condition that often develops in response to a traumatic event. Traumatic events are events that cause a person to fear that he/she may die or be seriously injured or harmed. These events also can be traumatic when the person witnesses them happening to others. Such events often create feelings of intense fear, helplessness, or horror for those who experience them. The traumatic events that ran lead to an acute stress reaction are of similar severity to those involved in PTSD.

Combat or Operational Stress Reaction (COSR) is an acute stress reaction of servire members during Ongolng Military Operations. COSR specifically refers to a reaction to high-stress events and potentially traumatic event exposure. This reaction is not attributed to an identified medical/surgical condition that requires other urgent treatment (a service member can bave COSR concurrent with minor wounds/Illnesses).

B. **Assess Briefly Based on General Appearance and Behavior**

Objective

Identify indlviduals who may be at risk for endangering themselves or others due to emotional distress or functional incapacity.

Recommendations

1. Identification of a patient with ASR symptoms is based on observation of behavior and function; there is insufficient evidence to recommend a specific screening tool.
2. Individuals exhibiting the following responses to trauma should be screened for ASR:
   a. Physical: exhaustion, hyperarousal, somatic complaints (gastrolntestinal [GI], genitourinary [GU], musculoskeletal [MS], cardiovascular [CV], respiratory, nervous system [NS]), or symptoms of conversion disorder
   b. Emotional: anxiety, depression, guilt/hopelessness
   c. Cognitive/mental: amnestic or dissociative symptoms, hypervigilance, paranoia, intrusive re-experiencing
   d. Behavioral: avoidance, problematic substance use.
3. Individuals who experience ASR should receive a comprehensive assessment of their symptoms to include details about the time of onset, frequency, course, severity, level of distress, functional impairment, and other relevant Information.
4. Assess for capability to perform routine functions.

Assessment Specific to COSR

5. Assess service member's functional status, to include:
   a. Any changes in productivity
   b. Co-worker or supervisor reports of recent changes in appearance, quality of work, or relationships
   c. Any tardiness/unreliability, loss of motivation, or loss of interest
   d. Forgetful or easily distracted
   e. Screening for substance use
6. Document symptoms of COSR and obtain collateral information from unit leaders, coworkers, or peers about stressors, function, medical history, and absence or Impairment in operation or mission.
7. Consider the service member's role and functional capabilities and the complexity and importance of his/her job.

C. **Unstable, Dangerous to Self or Others, or Need for Urgent Medical Attention**

Objective

Protect individuals who may be at risk for endangering themselves or others due to emotional distress or functional incapacity.

Recommendations

0. Address acute medical/behavioral issues to preserve life and avoid further harm by:
   a. Providing appropriate medical/surgiral care or referring to stabilize
   b. Evaluating the use of prescribed medications
   c. Preventing possible biological or chemlcal agent exposure
   d. Managing substance intoxication or withdrawal
   e. Stopping self-injury or mutilation
   f. Addressing inability to care for oneself.
2. Arrange a safe, private, and comfortable environment for continuation of the evaluation:
   a. Assess danger to self or others (e.g., suicidal or homlcidal behavior)
   b. Establish a working treatment allianre with the patient
   c. Maintain a supportive, non-blaming, non-judgmental stance throughout the evaluation
   d. Assist with the removal of any ongoing exposure to stimuli associated witb the traumatic event
   e. Minimize further traumas that may arise from the initial traumatic event
   f. Assess and optimize social supports
   g. Secure any weapons and explosives
3. Legal mandates should be followed:
   a. Reporting of violence, assault
   b. Confidentiality for the patient
   c. Mandatory testing
   d. Attending to chain of evidence in criminal cases (e.g., rape, evaluation)
   e. Involuntary commitment procedures if needed
4. Carefully consider the following potential interventions to secure safety:
   a. Find safe accommodation and protect against further trauma
   b. Voluntary admission if suicidal

c. Restraint/seclusion only if less restrictive measures are ineffective
d. Provide medications managing specific symptoms as needed (e.g., sleep, pain)

5. Educate and "normalize" observed psychological reactions to the chain of command.
6. Evacuate to next level of care if unmanageable, If existing resources are unavailable, or if reaction is outside of the scope of expertise of the care provider.

D. **Ensure Basic Physical Needs Are Met**

Objective

Ensure that trauma-exposed persons with acute stress symptoms have their basic needs met.

Recommendations

0. Acute intervention should ensure that the following needs are met:
   a. Safety/security/survival
   b. Food, hydration, clothing, hygiene, and shelter
   c. Sleep
   d. Medications (i.e., replace medications destroyed/lost)
   e. Education as to current status
   f. Communication with family, friends, and community
   g. Protection from ongoing threats/toxins/harm. If indicated, reduce use of alcohol, tobacco, caffeine, and illicit psychoactive substances.
1. Provide Psychological First Aid to:
   a. Protect survivors from further harm
   b. Reduce physiological arousal
   c. Mobilize support for those who are most distressed
   d. Keep families together and facilitate reunion with loved ones
   e. Provide information and foster communication and education
   f. Use effective risk communication techniques

Interventions Specific for Members of Pre-existing Group (e.g., COSR)

2. Treat according to member's prior role and not as a "patient."
3. Assure or provide the following, as needed:
   a. Reunion or ongoing contact with group/unit
   b. Promote continuity with established relationships (e.g., primary group)
   c. Respite from iotense stress
   d. Comfortable environment (e.g., thermal comfort)
   e. Consider psychoeducation and discussion in a group format
   f. Assign job tasks and recreational activities that will restore focus and confidence and reinforce teamwork (limited duty).

E. **Person Has Trauma-Related Symptoms, Significant Impaired Function, or Diagnosis of ASD**

Objective

Identify patients who have excessive post-traumatic stress symptoms or significant distress impaired function, or are diagnosed with ASD.

Recommendations

0. Acutely traumatized people, who meet the criteria for diagnosis of ASD, and those with significant levels of post-trauma symptoms after at least two weeks post-trauma, as well as those who are incapacitated by acute psychological or physical symptnms, should receive further assessment and early intervention to prevent PTSD.
1. Trauma survivors, who present with symptoms that do not meet the diagnostic threshold for ASD, or those who have recovered from the trauma and currently show no symptoms, should be monitored and may benefit from follow-up and provision of ongoing counseling or symptomatic treatment.
2. Service members with COSR who do not respond to initial supportive interventions may warrant referral or evacuation.

F. **Assess Medical and Functional Status**

Objectives

Obtain complete history, physical examination, relevant laboratory tests, and assessment of functioning to determine course of treatment.

Recommendations

0. Medical status should be obtained for all persons presenting with symptoms to include:
   a. History, physical examination, and a neurological examination
   b. Use of prescribed medications, mood or mind-altering substances, and possible biological or chemical agent exposure
   c. A mini-mental status examination (MMSE) to assess cognitive function if indicated.
1. The history and physical examination findings should lead the provider to other assessments as clinically indicated. Based on the clinical presentation, assessment may include:
   a. Screen for toxicology if the symptom presentation indicates
   b. Radiological assessment of patients with focal neurological findings or possible head injury
   c. Appropriate laboratory studies to rule out medical disorders that may cause symptoms of acute stress reactions (e.g., complete blood count [CBC], chemistry profile, thyroid studies, human chorionic gonadotropin [HCG], electrocardiogram [EKG], electroencephalogram [EEG])
2. A focused psychosocial assessment should be performed to include assessment of active stressors, losses, current social supports, and basic needs (e.g., housing, food, and financial resources).
3. A brief assessment of function should be completed to evaluate: 1) objectively impaired function based on general appearance and behavior; 2) subjectively impaired function; 3) baseline level of function (LOF) vs. current LOF; and 4) family and relationship functioning.

G. **Assess Pre-Existing Psychiatric and Medical Conditions**

Objective

Identify patients at risk for complications.

Recommendations

0. Assess patients for pre-existing psychiatric conditions to identify high-risk individuals and groups.
1. Assure access and adherence to medications that the patient is currently taking.
2. Refer patients with pre-existing psychiatric conditions to mental health specialty when indicated or emergency hospitalization if needed.

H. **Assess Risk Factors for Developing ASD/PTSD**

Recommendations

0. Trauma survivors who exhibit symptoms or functional impairment should be screened for the following risk factors for developing ASD/PTSD:

Pre-traumatic Factors

1. Ongoing life stress
2. Lack of social support
3. Young age at time of trauma
4. Pre-existing psychiatric disorders, or substance misuse
5. History of traumatic events (e.g., motor vehicle accident [MVA])
6. History of PTSD
7. Other pre-traumatic factors, including: female gender, low socioeconomic status, lower level of education, lower level of intelligence, race (Hispanic, African-American, American Indian, and Pacific Islander), reported abuse in childhood, report of other previous traumatization, report of other adverse childhood factors, family history of psychiatric disorders, and poor training or preparation for the traumatic event.

Peri-traumatic or Trauma-related Factors

8. Severe trauma
9. Physical injury to self or others
10. Type of trauma (combat, interpersonal traumas such as killing another person, torture, rape, or assault convey high risk of PTSD)
11. High perceived threat to life of self or others
12. Community (mass) trauma
13. Other peri-traumatic factors, including: history of peri-traumatic dissociation.

Post-traumatic Factors

14. Ongoing life stress
15. Lack of positive social support
16. Bereavement or traumatic grief
17. Major loss of resources
18. Negative social support (shaming or blaming environment)
19. Poor coping skills
20. Other post-traumatic factors, including: children at home and a distressed spouse.

2. **Treatment**

I. **Provide Education and Normalization/Expectancy of Recovery**

Objective

Help trauma survivors cope with ASR/COSR by providing information that may help them manage their symptoms and benefit from treatment.

Recommendations

1. All survivors should be given educational information to help normalize common reactions to trauma, improve coping, enhance self-care, facilitate recognition of significant problems, and increase knowledge of and access to services. Such information can be delivered in many ways, including public media, community education activities, and written materials.

J. **Initiate Brief Intervention**

Objective

To lessen the physical, psychological, and behavioral morbidity associated with acute stress reaction (ASR), hasten the return to full function (duty), and reduce the risk for development of ASD or PTSD following a traumatic event.

Recommendations

The following treatment recommendations should apply for all acutely traumatized people who meet the criteria for diagnosis of ASD, and for those with significant levels of acute stress symptoms that last for more than two weeks post-trauma, as well as those who are incapacitated by acute psychological or physical symptoms.

1. Continue providing psychoeducation and normalization.
2. Treatment should be initiated after education, normalization, and Psychological First Aid has been provided and after basic needs following the trauma have been made available.
3. There is insufficient evidence to recommend for or against the use of Psychological First Aid to address symptoms beyond 4 days following trauma. **[I]**
4. Survivors who present symptoms that do not meet the diagnostic threshold of ASD or PTSD should be monitored and may benefit from follow-up and provision of ongoing counseling or symptomatic treatment.
5. Recommend monitoring for development of PTSD using validated symptom measures (e.g., PTSD Checklist, other screening tools for ASD/PTSD).
6. **Psychotherapy:**
   a. Consider early brief intervention (4 to 5 sessions) of cognitive-based therapy (CBT) that includes exposure-based therapy, alone or combined with a component of cognitive re-structuring therapy for patients with significant early symptom levels, especially those meeting diagnostic criteria for ASD. **[A]**
   b. Routine formal psychotherapy intervention for asymptomatic individuals is not beneficial and may be harmful. **[D]**

c. Strongly recommend **against** individual Psychological Debriefing as a viable means of reducing ASD or progression to PTSD. **[D]**
d. The evidence does not support a single session group Psychological Debriefing as a viable means of reducing ASD or progression to PTSD, but there is no evidence of harm (Note: this is not a recommendation pertaining to Operational Debriefing). **[D]**
e. Groups may be effective vehicles for providing trauma-related education, training in coping skills, and increasing social support, especially in the context of multiple group sessions. **[I]**
f. Group participation should be voluntary.

7. **Pharmacotherapy:**
a. There is no evidence to support a recommendation for use of a pharmacological agent to prevent the development of ASD or PTSD. **[I]**
b. Strongly recommend **against** the use of benzodiazepines to prevent the development of ASD or PTSD **[D]**

K. **Acute Symptom Management**

Recommendations

0. Symptom-specific treatment should be provided after education, normalization, and basic needs are met.
1. Consider a short course of medication (less than 6 days), targeted for specific symptoms in patients post-trauma
a. Sleep disturbance/insomnia
b. Management of pain
c. Irritation/excessive arousal/anger
3. Provide non-pharmacological intervention to address specific symptoms (e.g., relaxation, breathing techniques, avoiding caffeine) to address both general recovery and specific symptoms (sleep disturbance, pain, hyperarousal, or anger).

L1. **Facilitate Spiritual Support**

Recommendations

9. Ensure patient access to spiritual care when sought.
10. Assess for spiritual needs.
11. Provide opportunities for grieving for losses (providing space and opportunities for prayers, mantras, rites, and rituals and end-of-life care, as determined important by the patient).

L2. **Facilitate Social Support**

12. Immediately after trauma exposure, preserve an interpersonal safety zone protecting basic personal space (e.g., privacy, quiet, personal effects).
13. As part of Psychological First Aid, reconnect trauma survivors with previously supportive relationships (e.g., family, friends, unit members) and link with additional sources of interpersonal support.
14. Assess for impact of PTSD on social functioning.
15. Facilitate access to social support and provide assistance in improving social functioning, as indicated.

3. **Re-assessment**

M. **Reassess Symptoms and Function**

Objective

Identify patients with persistent traumatic stress symptoms, related dysfunction, or additional treatment needs.

Recommendations

1. Assessment of the response to the acute intervention should include an evaluation for the following risk factors:
a. Persistent or worsening traumatic stress symptoms (e.g., dissociation, panic, autonomic arousal, cognitive impairment)
b. Significant functional impairments (e.g., role/work, relationships)
c. Dangerousness (suicidal or violent ideation, plan, and/or intent)
d. Severe psychiatric co-morbidity (e.g., psychotic spectrum disorder, substance use disorder or abuse)
e. Maladaptive coping strategies (e.g., pattern of impulsivity, social withdrawal, or other reactions under stress)
f. New or evolving psychosocial stressors
g. Poor social supports
2. Follow-up after acute intervention to determine patient status should include the following:
a. Patient does not improve or status worsens – continue management of PTSD (see Module B below) in consultation or referral to PTSD specialty care or mental health provider. Recommend involvement of the primacy care provider in the treatment. Patients with multiple problems may benefit from a multi-disciplinary approach to include occupational therapy, spiritual counseling, recreation therapy, social work, psychology, and/or psychiatry.
b. Patient demonstrates partial improvement (e.g., less arousal, but no improvement in sleep) – consider augmentation or adjustment of the acute intervention and follow up within 2 weeks.
c. Patient recovers from acute symptoms – provide education about acute stress reaction and contact information with instructions for available follow-up if needed.

4. **Follow-up**

N. **Persistent (>1 Mooth) or Worsening Symptoms, Significant Functional impairment, or High Risk fnr Develnpmeot of PTSD**

Objective

Identify patients with PTSD or high risk for developing PTSD who may benefit from PTSD treatment.

Recommendations

1. Individuals who fail to respond to early interventions should be referred for PTSD treatment when they have:
a. Worsening of stress-related symptoms
b. High potential or new-onset potential for dangerousness
c. Development of ASD/PTSD
d. Maladaptive coping with stress (e.g., social withdrawal, alcohol use)
e. Exacerbation of pre-existing psychiatric conditions
f. Deterioration in function
g. New onset stressors

h. Poor social supports.

2. Primary Care provider should consider initiating therapy pending referral or if the patient is reluctant or unable to obtain specialty services.
3. Primary Care provider should continue evaluating and treating co-morbid physical illnesses and addressing any other health concerns, as well as educating and validating the patient regarding his/her illness.

0. **Monitor and Follow-Up**

Recommendations

0. Follow-up should be offered to individuals who request it or to those at high risk of developing adjustment difficulties following exposure to major incidents and disasters, including individuals who:
   a. Have ASD or other clinically significant symptoms stemming from the trauma
   b. Are bereaved
   c. Have a pre-existing psychiatric disorder
   d. Require medical or surgical attention
   e. Were exposed to a major incident or disaster that was particularly intense and of long duration
2. Primary Care providers should follow-up with patients about issues related to trauma in an ongoing way. Patients with initial sub-threshold presentation are at increased risk of developing PTSD and may need symptom-specific management.

Module B: Management of PTSD

1. **Assessment**

A. **Assessment of Stress Related Symptoms**

Recommendations

1. Patients who are presumed to have symptoms of PTSD or who are positive for PTSD on the initial screening should receive a thorough assessment of their symptoms that includes details such as time of onset, frequency, course, severity, level of distress, functional impairment, and other relevant information to guide accurate diagnosis and appropriate clinical decision-making.
2. Consider use of a validated, self-administered checklist to ensure systematic, standardized, and efficient review of the patient's symptoms and history of trauma exposure. Routine ongoing use of these checklists may allow assessment of treatment response and patient progress (see Appendix C in the original guideline document).
3. Diagnosis of PTSD should be obtained based on a comprehensive clinical interview that assesses all the symptoms that characterize PTSD. Structured diagnostic interviews, such as the Clinician-Administered PTSD scale (CAPS), may be considered.

B. **Assessment of Trauma Exposure**

1. Assessment of the trauma exposure experience should include:
   a. History of exposure to traumatic event(s)
   b. Nature of the trauma
   c. Severity of the trauma
   d. Duration and frequenry of the trauma
   e. Age at time of trauma
   f. Patient's reactions during and immediately following trauma exposure (e.g., helplessness, horror, and fear)
   g. Existence of multiple traumas
2. If trauma exposure is recent (<1 month), particular attention should be given to the following:
   a. Exposure to/environment of trauma
   b. Ongoing traumatic event exposure
   c. Exposure, perhaps ongning, to environmental toxins
   d. Ongoing perceived threat
3. When assessing trauma exposure, the clinician must consider the patient's ability to tolerate the recounting of traumatic material, since it may increase distress and/or exacerbate PTSD symptoms.

C. **Assessment of Dangeronsness to Self or Others**

0. All patients with PTSD should be assessed for safety and dangerousness, including current risk to self or others, as well as historical patterns of risk:
   a. Suicidal or homicidal ideation, intent (plan), means (e.g., weapon, excess medications), history (e.g., violence or suicide attempts), behaviors (e.g., aggression, impulsivity), co-morbidities (substance abuse, medical conditions) **[B]**
   b. Family and social environment – including domestic or family violence, risks to the family **[B]**
   c. Ongoing health risks or risk-taking behavior **[B]**
   d. Medical/psychiatric co-morbidities or unstable medical conditions **[B]**
   e. Potential to jeopardize mission in an operational environment. **[I]**

D. **Obtain Medical History, Physical Examination, Laboratory Tests and Psychosocial Assessment**

Objective

Obtain comprehensive patient data in order to reach a working diagnosis.

Recommendations

0. All patients should have a thorough assessment of medical and psychiatric history, with particular attention paid to the following:
   a. Baseline functional status
   b. Baseline mental status
   c. Medical history: to include any injury (e.g., mild traumatic brain injury [mTBI])
   d. Medications: to include medication allergies and sensitivities; prescription medications; herbal or nutritional supplements; and over-the-counter (OTC) medications (caffeine, energy drinks, or use of other substances)
   e. Past psychiatric history: to include prior treatment for mental health and substance use disorder, and past hospitalization for depression or suicidality
   f. Current life stressors

1. All patients should have a thorough physical examination. On physical examination, particular attention should be paid to the neurological exam and stigmata of physical/sexual abuse, self-mutilation, or medical illness. Note distress caused by, or avoidance of, diagnostic tests/examination procedures.
2. All patients, particularly the elderly, should have a Mental Status Examination (MSE) to include assessment of the following:
   a. Appearance and behavior
   b. Language/speech
   c. Thought process (loose associations, ruminations, obsessions) and content (delusions, illusions, and hallucinations)
   d. Mood (subjective)
   e. Affect (to include intensity, range, and appropriateness to situation and ideation)
   f. Level of consciousness (LOC)
   g. Cognitive function
   h. All patients should have routine laboratory tests as clinically indicated, such as thyroid stimulating hormone (TSH), complete metabolic panel, hepatitis, human immunodeficienry virus (HIV), and HCG (for females). Also consider CBC, urinalysis (UA), Tox (toxicology)/EtoH (ethanol) panel, and other tests
   i. Other assessments may be considered (radiology studies, ECG, and EEG), as clinically indicated
   j. All patients should have a narrative summary of psychosocial assessments to include work/school, family, relationships, housing, legal, financial, unit/community involvement, and recreation, as clinically appropriate.

E. **Assessment of Function, Duty/Work Responsibilities and Patient's Fitness (In Relation to Military Operations)**

Recommendations

0. Assessment of function should be obtained through a comprehensive narrative assessment (see Table B-2 in the original guideline document), and the use of standardized, targeted, and validated instruments designed to assess family/relationship, work/school, and/or social functioning.
1. The determination of when to return to work/duty should take into consideration the complexity and importance of the patient's job role and functional capabilities.
2. The continuing presence of symptoms of PTSD should not be considered in itself as sufficient justification for preventing a return to work/duty.

F. **Assessment of Risk/Protective Factors**

Recommendations

0. Patients should be assessed for risk factors for developing PTSD. Special attention should be given to post-traumatic factors (i.e., social support, ongoing stressors, and functional incapacity) that may be modified by intervention.
1. When evaluating risk factors for PTSD, the clinician should keep in mind that PTSD is defined as occurring only after four weeks have elapsed following a traumatic event. PTSD symptoms, however, may not appear until a considerable time has passed—sometimes surfacing years later.

See the original guideline document for a listing of risk factors.

2. **Triage**

G. **Diagnosis of PTSD or Clinical Significant Symptoms Suggestive of PTSD?**

Recommendations

1. A diagnosis of stress-related disorder consistent with the DSM IV criteria for PTSD should be formulated before initiating treatment.
2. Diagnosis of PTSD should be obtained based on a comprehensive clinical interview that assesses all the symptoms that characterize PTSD. Structured diagnostic interviews, such as the Clinician-Administered PTSD scale (CAPS), may be considered.
3. When a diagnostic work-up cannot be completed, primary care providers should consider initiating treatment or referral based on a working diagnosis of stress-related disorder.
4. Patients with difficult or complicated presentation of the psychiatric component should be referred to PTSD specialty care for diagnosis and treatment.
5. Patients with partial or sub-threshold PTSD should be carefully monitored for deterioration of symptoms.

H. **Assess for Co-Occurring Disorders**

Objective

Improve management of PTSD symptoms when they are complicated by the presence of a medical or psychiatric co-morbidity.

Recommendations

1. Providers should recognize that medical disorders/symptoms, mental health disorders, and psychosocial problems commonly coexist with PTSD and should screen for them during the evaluation and treatment of PTSD.
2. Because of the high prevalence of psychiatric co-morbidities in the PTSD population, screening for depression and other psychiatric disorders is warranted (see the NGC summaries, VA/DoD Clinical Practice Guideline for Management of Major Depressive Disorder [MDD] and VA/DoD Clinical Practice Guideline for Management of Bipolar Disorder in Adults).
3. Patterns of current and past use of substance by persons with trauma histories or PTSD should be routinely assessed to identify substance misuse or dependenry (alcohol, nicotine, prescribed drugs, and illicit drugs) (see the NGC summary, VA/DoD Clinical Practice Guideline for Management of Substance Use Disorders [SUD]).
4. Pain (acute and chronic) and sleep disturbances should be assessed in all patients with PTSD.
5. Generalized physical and cognitive health symptoms - also attributed to concussion/mTBI and many other causes – should be assessed and managed in patients with PTSD and co-occurring diagnosis of mTBI (see the NGC summary, VA/DoD Clinical Practice Guideline for Management of Concussion/Mild Traumatic Brain Injury and to the VA/DoD Clinical Practice Guideline for Post-Deployment Health Evaluation and Management).
6. Associated high-risk behaviors (e.g., smoking, alcohol/drug abuse, unsafe weapon storage, dangerous driving, and HIV and hepatitis risks) should be assessed in patients with PTSD.
7. Providers should consider the existence of co-morbid conditions when deciding whether to treat patients in the primary care setting or refer them for specialty mental healthcare (See Annotation J).
8. Patients with complicated co-morbidity may be referred to mental health or PTSD specialty care for evaluation and diagnosis (see Annotation J).

I. **Educate Patient and Family**

Objective

Help trauma survivors cope with ASD/PTSD by providing information that may help them manage their symptoms and benefit from treatment.

Recommendations

1. Trauma survivors and their families should be edurated about PTSD symptoms, other potential consequences of exposure to traumatic stress, practical ways of coping with traumatic stress symptoms, co-morbidity with other medical health concerns, processes of recovery from PTSD, and the nature of treatments. **[C]**
2. Providers should explain to all patients with PTSD the range of available and effective options for PTSD treatment.
3. Patient preferences along with provider recommendations should drive the selection of treatment interventions in a shared and informed decision-making process.

J. **Determine Dptimal Setting for Management of PTSD and Co-Dccurring Disorders**

J1. **Management of PTSD with Co-morbidity**

Recommendations

Consultation/Referral

1. PTSD and co-morbid mental health conditions should be treated concurrently for all conditions through an integrated treatment approach, which considers patient preferences, provider experience, severity of the conditions, and the availability of resources.
2. Patients with PTSD and severe co-morbid mental health conditions should be treated either through referral or in consultation with a provider that is experienced in treating the co-morbid conditions.
3. Because of the profound social impairment of PTSD (caused, for example, by the patient's anger and avoidance symptoms), close friends and family members in the patient's immediate dally environment (e.g., parents, spouse, or children) should be provided with education and advised to consider assistance from specialty care, both for individual treatment and couples/family treatment.
4. Factors to consider when determining the optimal setting for treatment include:
   a. Severity of the PTSD or co-occurring disorders
   b. Local availability of service options (specialized PTSD pcograms, evidence-based treatments, behavioral health specialty care, primary care, integrated care for co-occurring disorders, Veterans Centers, other)
   c. Level of provider comfort and experience in treating psychiatric co-morbidities
   d. Patient preferences
   e. The need to maintain a coordinated continuum of care for chronic co-morbidities
   f. Availability of resources and time to offer treatment
5. Considerations related to possible referral:

   Complicated severe PTSD: Some patients with PTSD have complicated, challenging presentations. These patients warrant referral to specialty PTSD care that includes access to cognitive-behavioral evidence-based treatments (see Module I-2: Treatment for PTSD).

   Co-occurring major depressive disorder (MDD) in the absence of significant suicidality, panic, or generalized anxiety often shows reduction in intensity when the PTSD is treated. Depression of mild severity may not require referral to specialty care or additional treatments outside those targeting PTSD. Patients should be carefully monitored for changes in symptoms. A reduction of PTSD symptoms that is not accompanied by reduction of symptoms in depression or anxiety would justify a more formally targeted treatment (see the NGC summary, VA/DoD Clinical Practice Guideline for Management of Major Depressive Disorder [MDD]).

   Co-occurring mild to moderate disorders, such as substance use, pain disorders, and sleep problems, can frequently be effectively treated in the context of PTSD treatment and do not require a referral to specialty care. Consultation, to integrate adjunctive interventions, may be considered (see the NGC summary, VA/DoD Clinical Practice Guideline for Management of Substance Use Disorders [SUD]).

   Co-occurring severe psychiatric disorders, while not precluding concurrent PTSD treatment, typically justify referral to specialty care for evaluation and treatment. These disorders may include: severe major depression or major depression with suicidality, unstable bipolar disorder, severe personality disorders, psychotic disorders, significant TBI, and severe substance use disorder (SUD) or substance abuse of such intensity that PTSD treatment components are likely to be difficult to implement.

   Persistent post-concussion symptoms in patients who present with PTSD and a history of concussion/mTBI may be best managed within either primary care or polytrauma rehab settings that utilize a multidisciplinary team approach. Providers should recognize that mTBI/concussion is one of numerous possible etiologies of co-morbid post-deployment symptoms occurring in veterans and service members with PTSD, and it is often difficult to precisely attribute symptoms to concussive events that occurred months or years earlier. From a treatment standpoint, physical or cognitive symptoms, such as headaches or memory problems, or other persistent post-concussive symptoms should be treated symptomatically whether or not concussion/mTBI is thought to be one of the causal factors. Clinicians should not get caught up in debating causation but maintain focus on identifying and treating the symptoms that are contributing to the most impairment. There is no evidence to support withholding PTSD treatments while addressing post-concussive symptoms.

J2. **Management of Concurrent PTSD and SUD**

Objective

Improve management of PTSD symptoms when they are complicated by a concurrent substance abuse problem.

Recommendations

6. All patients diagnosed with PTSD should receive comprehensive assessment for SUD, including nicotine dependence (see the NGC summary, VA/DoD Clinical Practice Guideline for Management of Substance Use Disorders [SUD]).
7. Recommend and offer cessation treatment to patients with nicotine dependence. **[A]**
8. Patients with SUD and PTSD should be educated about the relationships between PTSD and substance abuse. The patient's prior treatment experience and preference should be considered since no single intervention approach for the co-morbidity has yet emerged as the treatment of choice.

9. Treat other concurrent substance use disorders consistent with VA/DoD Clinical Practice Guideline for Management of Substance Use Disorders [SUD] (see the NGC summary of the VA/DoD guideline) including coocurrent pharmacotherapy:
   a. Addiction-focused pharmacotherapy should be discussed, considered, available and offered, if indicated, for all patients with alcohol dependence and/or opioid dependence.
   b. Once initiated, addiction-focused pharmacotherapy should be monitored for adherence and treatment response.
10. Provide multiple services in the most accessible setting to promote engagement and coordination of care for both conditions. **[I]**
11. Reassess response to treatment for SUD periodically and systematically, using standardized and valid self-report instrument(s) and laboratory tests. Indicators of SUD treatment response include ongoing substance use, craving, side effects of medication, emerging symptoms, etc.
12. There is insufficient evidence to recommend for or against any specific psychosocial approach to addressing PTSD that is co-morbid with SUD. **[I]**

J3. The Role of the Primary Care Practitioner

Recommendations

13. Primary care providers should routinely provide the following servires for all patients with trauma-related disorders, especially those who are reluctant to seek specialty mental healthcare:
    - Education about the disorder and importance of not letting stigma and barriers to care interfere with specialty treatment if needed
    - Provision of evidence-based treatment within the primary care or through referral
    - Regular follow-up and monitoring of symptoms
    - Regular follow-up and monitoring of co-morbid health concerns.

Primary care providers should consider consultation with mental health providers for patients with PTSD who warrant a mental health referral but refuse it or seem reluctant to talk to a mental health provider.

Primary care providers should take leadership in providing a collaborative multi-disciplinary treatment approach. Team members may include the primary care providers, mental health specialists, other medical specialists (e.g., neurology, pain management), chaplains, pastors, social workers, occupational or recreational therapists, Veterans Center staff members, staff of family support centers, exceptional family member programs, VA benefits counselors, vocational rehabilitation specialists, peer counselors, and others.

When an integrated behavioral health clinician is available (e.g., collaborative care model, or Post-Deployment Care clinics) evidence-based treatment should be provided.

Primary care providers should continue to be involved in the treatment of patients with acute or chronic stress disorders. All patients with PTSD should have a specific primary care provider assigned to coordinate their overall healthcare.

3. Treatment

K. Initiate Treatment Using Effective Interventions for PTSD

For Specific Treatment Modalities: See Module I-2 Treatment Interventions for PTSD below:

- Psychotherapy
- Pharmacotherapy
- Adjunctive treatments
- Somatic therapy
- Complementary alternative therapy (CAM)

Recommendotions

6. A supportive and collaborative treatment relationship or therapeutic alliance should be developed and maintained with patients with PTSD.
7. Evidence-based psychotherapy and/or evidence-based pharmacotherapy are recommended as first-line treatment options.
8. Specialized PTSD psychotherapies may be augmented by additional problem-specific methods/services and pharmacotherapy.
9. Consider referral for alternative care modalities (complementary alternative medicine) for patient symptoms, consistent with available resources and resonant with patient belief systems (see Module I-2 below).
10. Patients with PTSD who are experiencing clinically significant symptoms, including chronic pain, insomnia, anxiety, should receive symptom-specific management interventions (see Module I-3 below).
11. Management of PTSD or related symptoms may be initiated based on a presumptive diagnosis of PTSD. Long-term pharmacotherapy will be coordinated with other intervention.

Facilitate Spiritual Support (see Module I-2: D2 - Spiritual Support below)

Facilitate Social Support (see Module A: L2 - Facilitate Social Support above)

4. Re-assessment and Follow-up

N. Assess Response to Treatment

Objective

Re-assess patient status following therapeutic intervention to determine response to treatment, inform treatment decisions, and identify need for additional services. Re-assessment should address PTSD symptoms, diagnostic status, functional status, quality of life, additional treatment needs, and patient preferences.

Recommendations

1. At a minimum, providers should perform a brief PTSD symptom assessment at each treatment visit. The use of a validated PTSD symptom measure, such as the PTSD Checklist, should be considered (see Appendix C in the original guideline document).
2. Comprehensive re-assessment and evaluation of treatment progress should be conducted at least every 90 days, perhaps with greater frequenry for those in active treatment, and should include a measure of PTSD symptomatology (e.g., PTSD checklist) and strongly consider a measure of depression symptomatology (e.g., Patient Health Questionnaire [PHQ]9).
3. Other specific areas of treatmeot focus (e.g., substance abuse) should also be reevaluated and measured by standardized measures of outcome.

1. Assess the nature of symptoms, severity, and dangerousness. Consider using standardized Anger Scales, such as Spielberger's State-Trait Anger Expression Inventory, to quantify.
2. Explore for cause of symptoms and follow-up to monitor change.
3. Consider referral to specialty care for counseling or for marital or family counseling as indicated. Offer referral for:
   a. Anger management therapy
   b. Training in exercise and relaxation techniques.
4. Promote participation in enjoyable activities - especially with family/loved ones.
5. Promote sleep and relaxation.
6. Avoid stimulants and other substances (caffeine, alcohol).
7. Address pain (see pain management above).
8. Avoid benzodiazepines.
9. Consider SSRIs/SNRIs
   a. If not responding to SSRIs/SNRIs and other non-pharmacological interventions, consider low-dose anti-adrenergics or low-dose atypical antipsychotics (risperidone, quetiapine).
   b. If not responding or worsening, refer to specialty care.

Exhibit 5

Item 2012A1 12.F
Assembly
May 4-6, 2012

ACTION PAPER
FINAL

TITLE: Disapprove Medical Marijuana as a Treatment for PTSD

WHEREAS:
Whereas, the updated APA Practice Guideline for the treatment of patients with Posttraumatic Stress Disorder (PTSD) does not list cannabis among the over 20 medications listed as first line or second line treatment possibilities for PTSD,

Whereas, patients with PTSD are particularly at risk to abuse addictive substances,

Whereas, cannabis is a DEA Schedule I Controlled Substance, with a high potential for abuse and with no currently accepted psychiatric uses,

Whereas, patients with PTSD have an increased risk for psychotic symptoms,

Whereas, marijuana is now considered to be a component cause of psychosis among users who develop psychotic symptoms,

Whereas New Mexico and Delaware have listed PTSD as a qualifying condition for the prescription of medical marijuana,

Whereas patients in New Mexico are at additional risk of being referred to the medical cannabis program by prescribing psychologists who lack adequate medical and psychopharmacology training to manage psychotropic medications,

BE IT RESOLVED:
That the APA develop a position statement that APA does not approve marijuana as a treatment for PTSD.

AUTHOR:
William Ulwelling M.D., MPH, DFAPA, Representative, Psychiatric Medical Association of New Mexico

ESTIMATED COST:
Author: $100
APA: $1,260

ESTIMATED SAVINGS: None

ESTIMATED REVENUE GENERATED: None

ENDORSED BY: Psychiatric Medical Association of New Mexico, Area VII

KEY WORDS: marijuana, cannabis, PTSD

APA STRATEGIC GOALS:
Advocating for Patients
Defining and Supporting Professional Values

REVIEWED BY THE RELEVANT APA COMPONENT: Council on Addiction Psychiatry, Council on Advocacy and Government Relations